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AN ANALYSIS OF THE DUODENAL DRAINAGE IN THE STEATORRHEAS

HERBERT F. PHILIPSBORN, JR., M.D., GRACE LAWRENCE, B.S., STANLEY GIBSON, M.D., AND HARRY GREENGARD, M.D., PH.D.
CHICAGO, ILL.

FIBROCYSTIC disease of the pancreas and celiac disease may resemble each other closely. The prognosis and management, however, are different; for this reason accurate diagnosis is desirable. Previous studies[1, 2, 3] have indicated that fibrocystic disease is characterized by an achylia or hypochylia pancreatica. Celiac disease, on the other hand, is considered a failure of absorption of already digested foodstuffs.[4]

A textbook comparison of the diseases may be readily constructed, but actual differentiation of the two conditions often is difficult. This paper is concerned with the diagnosis of fibrocystic and celiac diseases by quantitative analysis of the duodenal drainage for enzymatic activity and by notation of the volumetric response of the pancreas to secretin or N/10 HCl. Other laboratory aids do not appear to have the diagnostic significance which can be attributed to this procedure.

In both celiac and fibrocystic disease the feces are apparently more variable in character and composition than we have been led to believe. The stool of either disease may resemble that of the other (Figs. 3 and 4). It does not follow that since celiac disease is a failure of absorption the stools must be rich in free fatty acids and soaps; nor is it true that because fibrocystic disease is characterized by an achylia or hypochylia pancreatica the stools are of necessity abundant in unsplit fats.[3] The total activity of the entire gastrointestinal tract, not one organ, determines the character of the stool. Fecal analysis may indicate whether or not a state of steatorrhea exists;[5] it will not point out its etiology.

The vitamin A absorption curve is both low and flat in fibrocystic disease; usually it remains under 30 units (Fig. 3). In celiac disease

From The Children's Memorial Hospital, and the Department of Physiology and Pharmacology, Northwestern University.

it may be somewhat higher (Fig. 4); however, like the glucose tolerance curve, it is apparently related to intestinal motility.[6, 7, 8] It would seem wise, therefore, to consider a low or flat vitamin A curve in the presence of foul, frothy stools as indicative of a sluggish and dilated bowel, the type which is commonly associated with the steatorrheic state.

Since the stools in celiac and fibrocystic disease may be identical and because the vitamin A curve is diagnostically nonspecific, the best evidence of pancreatic function is obtained by determination of enzymatic activity in the duodenal drainage. Further diagnostic aid may be obtained by noting the response to intraduodenal N/10 HCl or intravenous secretin.

Material.—The children studied have readily fallen into four groups: (a) normal children, (b) children considered "feeding problems," (c) children with fibrocystic disease, and (d) children with celiac disease. Children called normal have been afebrile, in a good state of nutrition, and free from any evidence of gastrointestinal disturbances. "Feeding problems" should more properly be called diagnostic enigmas; they had failed to gain weight and maintain an adequate state of nutrition in spite of the fact that they were free from any apparent pathologic process when hospitalized. Those considered to have fibrocystic disease fell into one of the categories previously described.[3] Three of the five children have radiologic evidence of pulmonary involvement. Two came to necropsy. The living patients have shown, at least temporarily, gastrointestinal improvement on substitution therapy. Celiac disease was considered to be present when either all or a large majority of the criteria by which Gee[9] first described the disease were present. Secretin was prepared by one of us (H. G.).

Methods.—At the time a feeding or meal would ordinarily be given, a Levine tube is passed through one of the nostrils into the pyloric antrum. When the tip of the tube is securely placed in the pyloric antrum the child is returned to bed and encouraged to drink a cup of water or fruit juice. No other foods or fluids are allowed. Approximately two hours later the position of the tube is determined by fluoroscopy. If the tip of the tube is not in the duodenum it is replaced in the pyloric antrum; the child is returned to bed and the procedure repeated. When the tip of the tube is seen to be in the second portion of the duodenum upon fluoroscopic examination in both anteroposterior and lateral positions the child is placed either in bed or upon an examining table. He is then entertained by play or reading as the material from the duodenum is collected. Often the child will fall asleep while the material is being collected. A few struggle until fatigued. The material from the duodenum flows out of the tube in waves of increased and decreased rates. It is usually a light golden yellow, barely alkaline in reaction, and may contain stringy, viscous, white material. Occa-

sionally the material flowing from the tube is colorless. The drainage should be collected in test tubes surrounded by ice. The material is gathered over a half-hour period. Then either from 10 to 15 mg. of secretin may be given intravenously, or 10 c.c. N/10 HCl administered intraduodenally and left there for ten minutes. Collection of the duodenal drainage is begun anew and continued over a period of time equal to the first collection. The volumes and the pH (nitrazine paper as indicator) of the samples are recorded and the clearest specimens of the greatest pH, obtained before and after pancreatic stimulation, are either analyzed immediately or frozen for subsequent studies.

Chemical Methods.—The tryptic activity of the duodenal drainage is measured by the amount of nitrogen liberated from a casein substrate. This is the Northrop and Kunitz[10] modification of the method of McClure, Wetmore, and Reynolds.[11] The duodenal fluid is diluted 1 to 25 with distilled water. One c.c. of diluted fluid is added to 5 c.c. of casein solution. This is incubated at 37° C. for sixty minutes at the end of which time the undigested casein is precipitated with 10 per cent trichloracetic acid. The mixture is filtered and an aliquot (5 c.c.) of clear filtrate is analyzed by the micro-Kjeldahl method.[12] Since the nonprotein nitrogen determined as described included that which is preformed in the reagents and duodenal juice as well as that which is produced by proteolytic action on the casein it is necessary to control each determination with a blank. This is accomplished by assaying, as aforementioned, a sample of the diluted duodenal fluid which has been inactivated by heating in boiling water for five minutes. The nitrogen content of the sample containing the inactivated trypsin is subtracted from that containing the active trypsin. The results are calculated as grams of nitrogen per 100 c.c. of duodenal juice.

Solutions.—(a) The phosphate mixture (pH 8.4) is made by adding 20 c.c. of potassium acid phosphate (27.234 Gm. to a liter) to 980 c.c. of a solution of disodium phosphate (35.628 Gm. per liter). (b) Casein solution is prepared by placing 1 Gm. of soluble casein in a dry flask and then adding 100 c.c. of phosphate mixture (pH 8.4). The casein is dissolved by quickly rotating the flask after having heated the solution to 57° C. When all of the casein is in solution, 4 c.c. of N/10 NaOH is added.

The amylolytic activity of the duodenal drainage is measured by the amount of dextrose formed from starch which has been digested by the duodenal contents over a given period of time. This is done according to McClure, Wetmore, and Reynolds'[11] modification of the method of Wohlgemuth.[13] The duodenal fluid is diluted 1 to 25 with a phosphate buffer mixture (pH 8.4). One c.c. of the duodenal contents and 9 c.c. of starch phosphate mixture are digested at 40° C. for 30 minutes. The liberated dextrose is then determined according to the method of

Folin and Wu.[14] Results are calculated in grams of dextrose per 100 c.c. of original duodenal contents.

Solutions.—(a) Phosphate mixture (pH 8.4) is prepared as previously described. (b) Starch phosphate mixture is prepared by adding 4 Gm. of soluble starch (Kahlbaum) to 100 c.c. of distilled hot water. This is then cooled and diluted with an equal volume of phosphate mixture.

Lipolytic activity of the duodenal contents is measured by the number of cubic centimeters of N/20 NaOH required to neutralize the free fatty acid liberated from an emulsion of homogenized olive oil. This is done according to a modification of the method of Cherry and Crandall.[15]

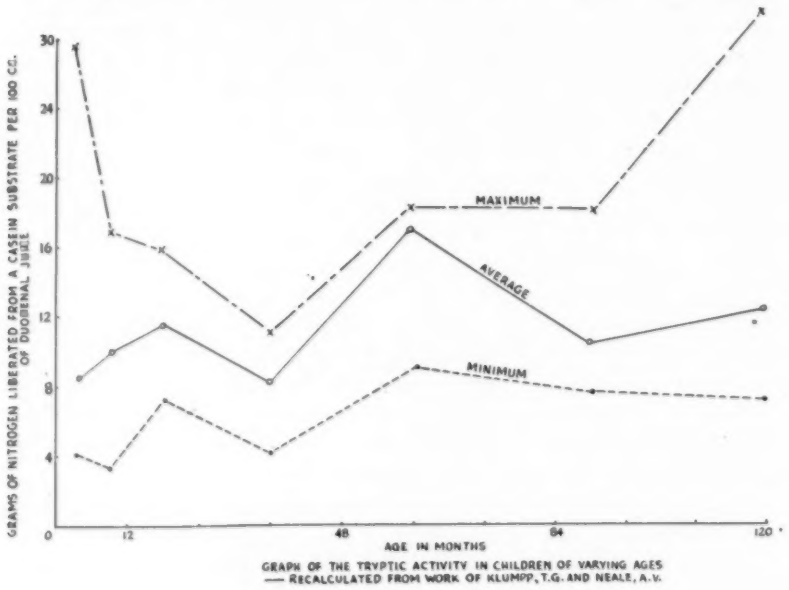

Fig. 1.

The duodenal contents are diluted 1 to 25 with a phosphate buffer (pH 7.0). Two cubic centimeters of olive oil emulsion, 1 c.c. of diluted duodenal juice, 3 c.c. of distilled water and ½ c.c. of phosphate buffer mixture (pH 7.0) are incubated at 37° C. for twenty-four hours. At the end of this time 3 c.c. of alcohol (95 per cent) is added and the mixture titrated with N/20 NaOH. As a control a boiled sample of the diluted duodenal juice is treated as described. The difference between the titration values of the boiled and unboiled samples expressed as cubic centimeters of N/20 NaOH is the index of lipolytic activity.

Solutions.—(a) Olive oil emulsion is prepared just before using by thoroughly mixing equal parts of a 1 per cent solution of gum acacia

and olive oil. (The olive oil must be free from fatty acids.) (b) Phosphate buffer mixture (pH 7.0) is prepared according to Sørenson.[16]

Results.—The fasting values obtained by analysis of the duodenal drainage of normal children closely resemble the results obtained by Klumpp and Neale[17] (Figs. 1 and 2 and Table I). Table I contains the results of analysis for enzymatic activity of the duodenal drainage of seven normal children. Fig. 5 shows the response to secretin in a normal child and contrasts it with the response noted in celiac and fibrocystic disease.

Children whom we have designated as "feeding problems" entered the hospital with a severe degree of malnutrition. Studies of the duodenal

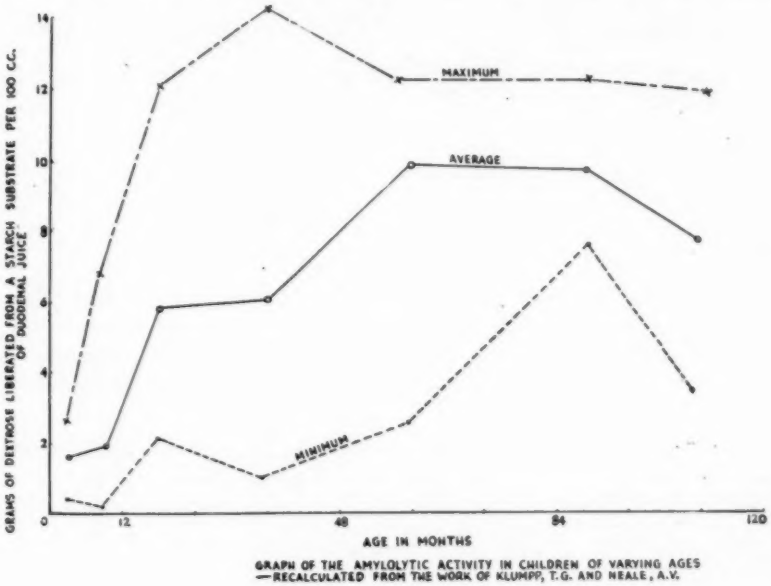

Fig. 2.

drainage revealed a marked hypochylia pancreatica. It is logical to assume that the pancreatic insufficiency that was noted upon hospitalization was only transient since all of these children have subsequently attained a satisfactory nutritional status on a general diet. Furthermore, one of them (M. C., Table II) was subjected to a second duodenal analysis approximately nine months after her original test and this time was found entirely normal.

Five patients with fibrocystic disease are presented in Table III and Fig. 3. It will be noted that the enzyme concentration in their duodenal drainage is either very low or absent. The typical loss of response to secretin is illustrated in Fig. 5.

TABLE I

DUODENAL ENZYMATIC ACTIVITY (NORMAL CHILDREN)

CASE	AGE (MO.)	t	a	l	Vb	Va	St
V. B.	5	9.5	2.6	146	18 c.c. pH 6.5	30 c.c. pH -	A
K. M.	13	10.4	8.7	111	28 c.c. pH 7.0	21 c.c.	A
F. M.	13	12.7	1.9	204	22 c.c. pH 6.5	25 c.c. pH 7.5	A
S. N.	13	14.6	9.3	206	8 c.c. pH 6.5	18 c.c. pH 7.0	A
R. B.	14	6.5	2.4	106	19 c.c. pH 6.0	44 c.c.	S
R. N.	36	7.9	9.4	23	25 c.c. pH 7.0	48 c.c. pH 7.0	A
V. S.	48	6.1	5.6	146	pH 7.0	----	O

In all cases except V. S. determinations were made of enzymatic values before and after pancreatic stimulation; only the maximal values are recorded.

Key:

t: Tryptic activity expressed in grams of liberated nitrogen per 100 c.c. duodenal juice

a: Amylolytic activity expressed in grams of liberated dextrose per 100 c.c. duodenal juice

l: Lipolytic activity expressed in cubic centimeters N/20 NaOH per 1 c.c. duodenal juice

Vb: Volume of duodenal drainage for one-half hour before pancreatic stimulation

Va: Volume of duodenal drainage for one-half hour after pancreatic stimulation

St: Type of pancreatic stimulus

S: Secretin

A: N/10 HCl

As would be expected from a study of the pathogenesis of celiac disease, the concentration of enzymes in the duodenal drainage is entirely normal (Table IV, Fig. 4). The volumetric response after stimulation of the pancreas by secretin indicates that there is no intrapancreatic block (Fig. 5).

Discussion.—Ten to fifteen years before Gee[9] described celiac disease, Zweifel[18] and later Korowin[19] studying the action of intestinal ferments came to the conclusion that there was little or no amylase in the duodenum of normal infants. These results have been substantiated by later investigators.[17]

TABLE II

DUODENAL ENZYMATIC ACTIVITY (FEEDING PROBLEMS)

CASE	AGE (MO.)	t	a	l
J. R.	4	0.07	--	0.5
T. H.	4	0.03	--	6.74
R. N.	6	0.37	--	9.96
M. C.	7	0.03	--	2.68
	16	14.7	7.85	173

Values determined with patient in a fasting state.

Key:

t: Tryptic activity expressed in grams of liberated nitrogen per 100 c.c. duodenal juice

a: Amylolytic activity expressed in grams of liberated dextrose per 100 c.c. duodenal juice

l: Lipolytic activity expressed in cubic centimeters N/20 NaOH per 1 c.c. duodenal juice

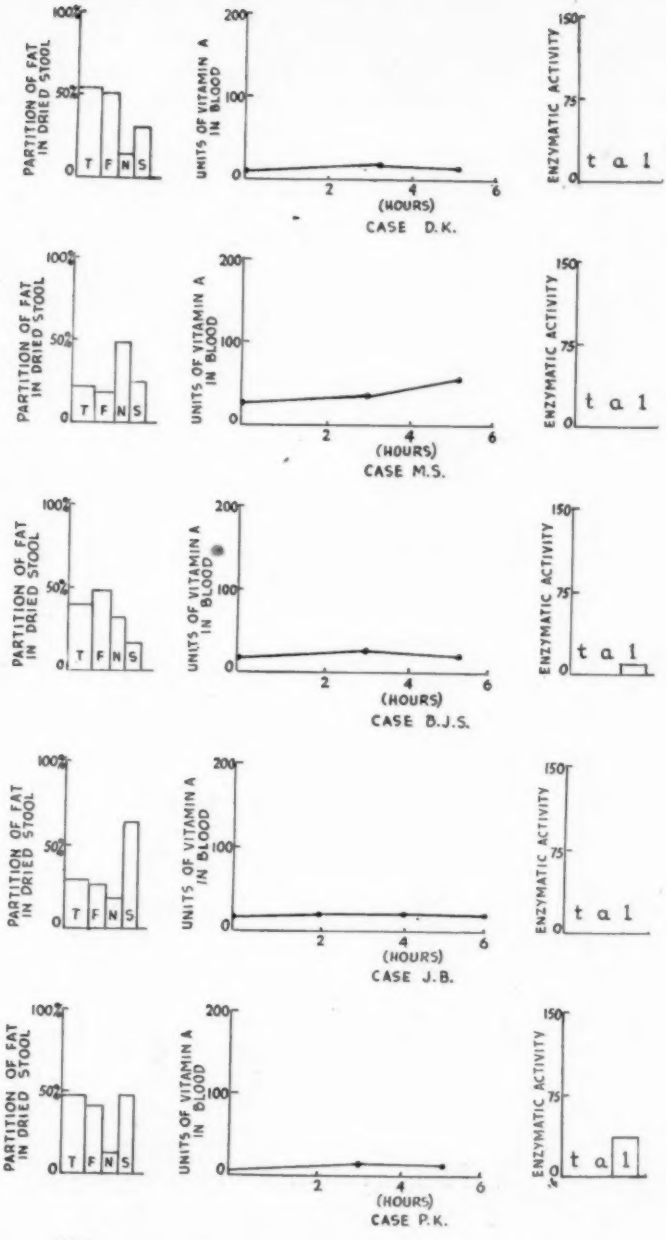

Fig. 3.—Fibrocystic disease of the pancreas.

In 1912 Hess discussed the technique of duodenal intubation in infants and young children.[20] His work in this field antedated the Einhorn tube[21] which was a potent stimulus to study of barely accessible

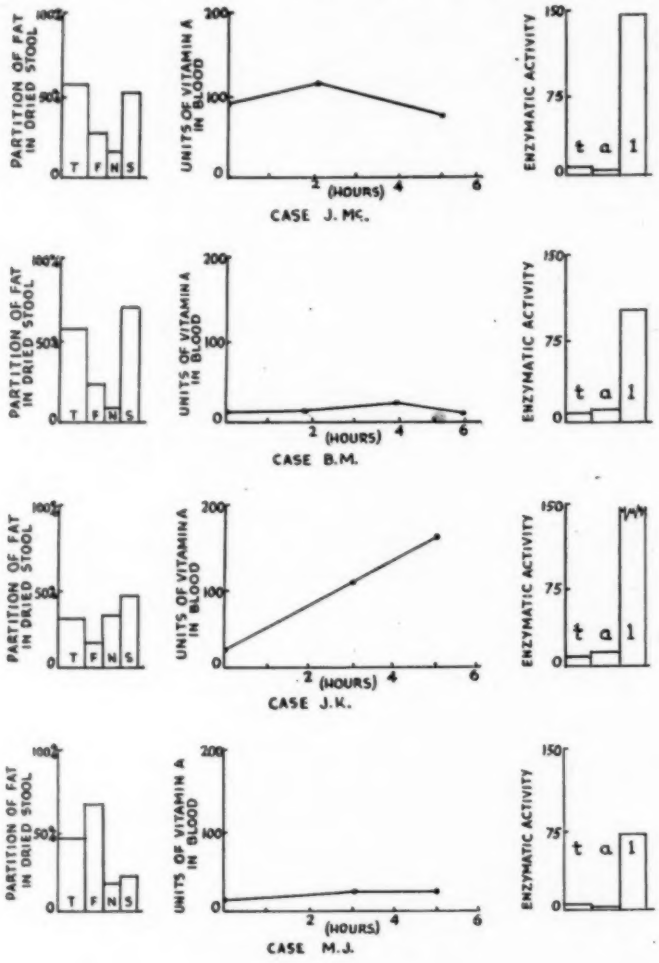

Fig. 4.—Celiac disease.

portions of the gastrointestinal tract. Today Hess's work has little practical value as his results were expressed qualitatively.

More recently Davison[22] studied the duodenal drainage of six normal infants and reported values for trypsin and amylase.

Klumpp and Neale[17] have studied the duodenal ferments of seventy-four normal children varying in age from 1 to 144 months. This is the only large series of children of whom we are aware in which the duodenal enzymes have been studied painstakingly and thoroughly. Unfortunately values for enzyme activity were expressed without regard for volume. Any attempt to use them for comparison with data obtained from study of other children must be done after re-expression

TABLE III

FIBROCYSTIC DISEASE

DUODENAL ENZYMATIC ACTIVITY

CASE	AGE (MO.)	t	a	l	Vb	Va	St
P. K.	2	1.2	0	30	5 c.c. pH 6.5	5 c.c. pH 6.5	S
J. B.	4	0	--	0	--	--	--
B. J. S.	15	0	.55	3.0	8 c.c. pH ?	6 c.c. pH ?	S
M. S.	19	0	--	1.75	Acid to litmus paper	--	--
D. K.	24	0	0	9	10 c.c. pH 5.0	6 c.c. pH 6.5	S

In cases where the pancreas was stimulated, determinations were made of enzymatic activity before and after stimulation; only the maximal values are recorded.
Key:

t: Tryptic activity expressed in grams of liberated nitrogen per 100 c.c. duodenal juice
a: Amylolytic activity expressed in grams of liberated dextrose per 100 c.c. duodenal juice.
l: Lipolytic activity expressed in cubic centimeters N/20 NaOH per 1 c.c. duodenal juice
Vb: Volume of duodenal drainage for one-half hour before pancreatic stimulation
Va: Volume of duodenal drainage for one-half hour after pancreatic stimulation
St: Type of pancreatic stimulus
S: Secretin
A: N/10 HCl

TABLE IV

CELIAC DISEASE

DUODENAL ENZYMATIC ACTIVITY

CASE	AGE (MO.)	t	a	l	Vb	Va	St
J. Mc	15	6.3	1.5	144	--	--	--
J. K.	22	10.2	1.4	228	10 c.c.	50 c.c.	S
M. J.	34	5.0	1.9	67.2	10 c.c.	15 c.c.	A Blood CO_2 content
	35	4.8	6.6	180	--	--	
B. M.	104	3.6	8.2	99	43 c.c. pH 7.0	60 c.c. pH 7.0	A

In all cases where the pancreas was stimulated, determinations were made of enzymatic activity before and after stimulation; only maximal values are recorded.
Key:

t: Tryptic activity expressed in grams of liberated nitrogen per 100 c.c. duodenal juice
a: Amylolytic activity expressed in grams of liberated dextrose per 100 c.c. duodenal juice
l: Lipolytic activity expressed in cubic centimeters N/20 NaOH per 1 c.c. duodenal juice
Vb: Volume of duodenal drainage for one-half hour before pancreatic stimulation
Va: Volume of duodenal drainage for one-half hour after pancreatic stimulation
St: Type of pancreatic stimulus
S: Secretin
A: N/10 HCl

of their results. We have done this and have an excellent estimate of the enzymatic activity in the duodenum of the normal child (Figs. 1, 2).

According to the re-expressed results of Klumpp and Neale[17] the amylolytic activity of the duodenal drainage is low during the first year of life after which time it rises steeply and then maintains a relatively constant value. Unfortunately amylolytic activity is most variable during early life when constancy is diagnostically desirable. If during the first year of life less than 0.5 Gm. of dextrose is liberated by 100 c.c. of duodenal juice, pancreatic amylase may be considered deficient. Likewise after 1 year of age, less than 2 Gm. of liberated dextrose may be considered abnormal.

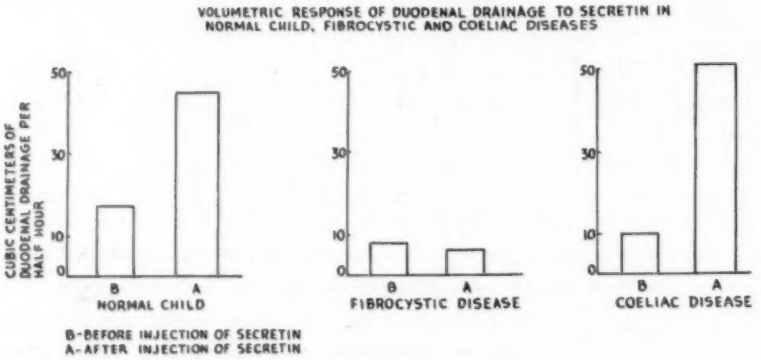

Fig. 5.

Determination of lipolytic activity is subject to a number of vagaries. At best the method is crude and the range of normal great. By the technique that we have employed[15] it has been felt that when less than 60 c.c. of N/20 NaOH is required to neutralize the free fatty acids liberated by 100 c.c. of duodenal drainage pancreatic lipase is deficient.

The tryptic activity of the duodenal drainage varies less with age than does the amylolytic activity. The accuracy by which it can be determined is far greater than that by which the activity of pancreatic lipase is measured. For these reasons an estimate of the tryptic activity in the duodenal drainage is the most reliable index of pancreatic function. Values of less than 4 Gm. of liberated nitrogen per 100 c.c. of duodenal juice may be considered abnormal. For practical purposes it is not necessary to determine lipolytic or amylolytic activity since the diminished pancreatic output of one enzyme is usually accompanied by a similar change in the output of the others.

An argument commonly advanced against the accuracy of judging pancreatic function by enzymatic activity of the duodenal drainage is that the activity of ferments derived from portions of the gastrointestinal

TABLE V

PANCREATIC INSUFFICIENCY WITH INFANTILISM

CASE	CHRONOLOGICAL AGE	SKELETAL AGE (CARPAL BONES)	TOTAL STOOL FAT—DRIED	VITAMIN A CURVE			t	a	l	Vb	Va	St
				F	3h	5h						
C.T.	4½ yr.	2½ yr.	32.6% or 4.9 Gm. per 24 hr.	19	93	100	1.5	.78	23	8 c.c. pH 7.0	24 c.c. pH 7.0	A

Only maximal values recorded.

Key:
F—Fasting vitamin A level
3h—3-hour vitamin A level
5h—5-hour vitamin A level
t—Tryptic activity expressed in grams of liberated nitrogen per 100 c.c. duodenal juice
a—Amylolytic activity expressed in grams of liberated dextrose per 100 c.c. duodenal juice
l—Lipolytic activity expressed in cubic centimeters N/20 NaOH per 1 c.c. duodenal juice
Vb—Volume of duodenal drainage for one-half hour before pancreatic stimulation
Va—Volume of duodenal drainage for one-half hour after pancreatic stimulation
St—Type of pancreatic stimulus
A—N/10 HCl

tract other than the pancreas is also measured. This is an obvious source of error which is not easily eliminated in clinical studies; however, the greater portion of the secretions present in the region of the pancreatic duct are under normal fasting conditions derived from the pancreas.[23] Furthermore, estimation of proteolytic activity, which is the most significant measure of pancreatic function, is conducted in alkaline media thus eliminating the possibility of measuring peptic activity.[24] Another criticism leveled against estimates of enzymatic activity as an index of pancreatic function is that the succus entericus, bile, and stomach contents dilute the pancreatic secretions producing subnormal values. This is a valid criticism. However, we make no claim to have studied unadulterated pancreatic fluid. To minimize the factor of dilution, precautions have been taken to examine the clearest specimen of the highest pH from each child; it is felt that this specimen contains less diluents than one which is more acid or deeply bile stained. We believe that by following these criteria we have studied the nearest approach to pure pancreatic fluid that can be obtained by use of a duodenal catheter. As a further precaution our results have been compared with those of Klumpp an Neale[17] who used similar technical and chemical methods (except for estimation of lipolytic activity).

The volumetric changes in the duodenal drainage after pancreatic stimulation by intravenous secretin or intraduodenal N/10 HCl have been of diagnostic value. Investigations have shown that the output of the normal pancreas is increased in response to intravenous secretin[25] or intraduodenal hydrochloric acid.[23]

In fibrocystic disease one would expect the response of the pancreas to secretin or acid to be obliterated since the pathology of the disease is

such that an intrapancreatic block exists. Actually this is what does occur (Fig. 5).

Fibrocystic disease is precluded no matter how little enzymatic activity is present in the duodenal drainage if a significant increase in the volume of the duodenal juice occurs after pancreatic stimulation. Such a response does not, however, rule out a nonspecific achylia or hypochylia pancreatica (Table V).

In celiac disease there are no demonstrable pathologic changes in the pancreas and as one would expect the response to pancreatic stimulation is similar to that seen in a normal child (Fig. 5).

CONCLUSIONS

1. The stools and vitamin A curves in celiac disease may closely resemble those in fibrocystic disease.

2. Quantitative analysis of the duodenal drainage for enzymatic activity coupled with a notation of the response of the pancreas to secretin or intraduodenal hydrochloric acid is the most reliable laboratory aid in the differential diagnosis of fibrocystic and celiac disease.

3. "Feeding problems" may be on the basis of a temporary pancreatic insufficiency.

4. Permanent pancreatic insufficiency with infantilism must be differentiated from celiac disease, fibrocystic disease, and certain types of feeding problems.

5. The value for tryptic activity is the most reliable index of pancreatic function. Values of less than 4 Gm. of liberated nitrogen per 100 c.c. of duodenal fluid are abnormal in children.

6. Less than 0.5 Gm. of liberated dextrose per 100 c.c. of duodenal drainage during the first twelve months of life is abnormal. Subsequently less than 2 Gm. of liberated dextrose is abnormal in children.

7. When less than 60 c.c. of N/20 NaOH is required to neutralize the free fatty acids produced by the lipolytic activity of 100 c.c. of duodenal fluid the pancreatic lipase may be considered diminished in children.

8. The enzymatic activity in the duodenal drainage is markedly diminished in fibrocystic disease; it remains essentially normal in celiac disease.

9. The response to intravenous secretin or intraduodenal N/10 HCl is reduced in fibrocystic disease but may remain normal in celiac disease, transient and permanent hypochylia pancreatica.

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REFERENCES

1. Andersen, D. H.: Am. J. Dis. Child. **63**: 643, 1942.
2. Maddock, C. L., Farber, S., and Shwachman, H.: Am. J. Dis. Child. **66**: 370, 1943.
3. Philipsborn, H., Lawrence, G., and Lewis, K.: J. PEDIAT. **25**: 284, 1944.

4. Bodansky, M., and Bodansky, O.: Biochemistry of Disease, New York, 1940, The Macmillan Company.
5. Andersen, D. H., in Brennemann's Practice of Pediatrics, Hagerstown, Md., 1944, W. F. Prior Company, vol. 1, chap. 29.
6. Breese, B. B., Jr., and McCoord, A.: Am. J. Pediat. **15**: 183, 1939.
7. May, C. D., and McCreary, J. F.: J. PEDIAT. **17**: 143, 1940.
8. Flax, L. J., Barnes, M., and Reichert, L. J.: J. PEDIAT. **21**: 475, 1942.
9. Gee, Samuel: St. Barth. Hosp. Rep. **34**: 17, 1888.
10. Northrop, J. H., and Kunitz, M. J.: Gen. Phys. **16**: 313, 1932.
11. McClure, C. W., Wetmore, A. S., and Reynolds, L.: Arch. Int. Med. **27**: 706, 1921.
12. Osgood, E. E.: Laboratory Diagnosis, Philadelphia, 1940, P. Blakiston's Son & Co.
13. Wohlgemuth, J.: Biochem. Ztschr. **9**: 1, 1908.
14. Folin, O., and Wu, H.: J. Biol. Chem. **38**: 81, 1919.
15. Cherry, I. S., and Crandall, L. A., Jr.: Am. J. Physiol. **100**: 266, 1932.
16. Clark, W. M.: The Determination of Hydrogen Ions, Baltimore, 1928, Williams and Wilkins Company.
17. Klumpp, T. G., and Neale, A. V.: Am. J. Dis. Child. **40**: 1215, 1930.
18. Zweifel: Untersuch, u.d. Verdauungsapparat d. Neugeb. 1874, p. 35 quoted by Hess, A. F.[20]
19. Korowin, J.: Jahrb. f. Kinderh. **3**: 342, 1898. Quoted by Hess.[20]
20. Hess, A. F.: Am. J. Dis. Child. **4**: 205, 1912.
21. Einhorn, M.: M. Rec. New York, 1910, No. 3.
22. Davison, W. C.: Am. J. Dis. Child. **29**: 743, 1925.
23. Thomas, J. E., and Crider, J. O.: Am. J. Physiol. **131**: 349, 1940.
24. MacLeod's Physiology in Modern Medicine, ed. 8, St. Louis, 1938, C. V. Mosby Company, p. 695.
25. Greengard, H., Stein, I. F., Jr., and Ivy, A. C.: Am. J. Physiol. **132**: 305, 1940.

OBSERVATIONS ON THE CHILD POPULATIONS, BIRTH AND INFANT DEATH RATES, AND MEDICAL PERSONNEL IN CERTAIN COUNTRIES

Major James B. Gillespie
Medical Corps, Army of the United States

THE government and peoples of the United States have frequently demonstrated concern for underprivileged peoples by their efforts to improve the situations of such groups. Whether the misfortunes of these groups have resulted from flood, earthquake, famine, or war the agencies, personnel, and supplies for relief have often been provided by this country. World War II, affecting people of all races in scattered countries, has created perhaps the greatest problem of relief and rehabilitation in history. In this conflict governments of the United States and other United Nations have had a special interest in the health and welfare of civil populations. This interest is not prompted merely by humanitarian instincts, but also by the fact that conditions of poor sanitation and high disease incidence among civilians are detrimental to the health of Allied troops stationed in the areas and, consequently, prejudicial to the war effort.

Prolonged dietary restriction, destruction of homes and sanitary facilities, lack of adequate medical care, and the psychological trauma of modern warfare have made definite and often permanent imprint upon the health of individuals in civil populations. It is unlikely that any age groups have been more adversely affected than infants, children, and adolescents. To anticipate the nature and probable extent of problems of health and welfare of the children in various countries, a knowledge of composition of populations as to age groups, birth and infant mortality rates, and adequacy and standards of prewar medical care is helpful. Such data, though modified by several years of war, provide an index to the type and extent of problems which may be anticipated. Moreover, knowledge of this type facilitates proper plans for relief and rehabilitation of these unfortunate younger groups.

COMPOSITION OF TOTAL POPULATION BY AGE GROUPS IN CERTAIN COUNTRIES

The number of infants and children among civilian populations determines to some degree the programs, personnel, and supplies necessary for relief. The age composition of a population is the creation of all factors affecting births, deaths, and migration from the birth of the oldest living inhabitant to the present time. The changes in structure of total populations are the cumulative result of the changes in age groups. Undoubtedly great changes in composition of total populations will result from the war. Since casualties are no longer confined to com-

From the Civil Public Health Division, The Preventive Medicine Service, Office of The Surgeon General, Washington, D. C.

bat troops on the battlefield, and with the increase in disease, lowered standards of living, malnutrition, and relaxation of public health control, reliable mortality figures cannot be estimated in certain countries. Also estimates of the unborn as a result of military mobilization are even less exact than estimates of mortality. Knowledge of loss of births, as well as loss of life, is essential to reasonably accurate estimations of structural changes in populations.[1]

The composition of total population by age groups in certain countries in the prewar period is indicated in Fig. 1. Data used to compile all charts were obtained from the most recent and accurate sources available.[2-7] Vital statistics for certain countries are less complete due to inadequate laws or enforcement measures pertaining to registration of births and deaths and the taking of census. In Far Eastern countries, excepting Japan, the less highly organized health departments, the relatively small group of trained medical personnel and the inadequate systems of communication favor less complete records. It is believed, despite possible inadequacies, prewar compositions of populations by age show characteristic features helpful to relief planning for the younger groups in various countries. For purposes of classification, children have been regarded as individuals less than 15 years of age, and they are arbitrarily grouped into four subdivisions according to age, namely: under 1 year, 1 through 4 years, 5 through 9 years, and 10 through 14 years.

Comment.—It will be noted that the proportion of infants and children in the Far East is generally greater than in other parts of the world. The Balkans have the greatest proportion of total populations under 15 years of age in Europe; the Scandinavian countries have the smallest. The young age groups form a greater proportion of total population in the United States than in most of the countries of Western Europe.

Since birth rates in Far Eastern countries are consistently high (see Fig. 2) it would be expected that the young age groups would be large. Because of large young age groups, the number of persons entering child-bearing age in the Far East is obviously great; a constant high birth rate is thus maintained. Relatively small adult groups in Far Eastern countries are accounted for by high birth rates and undoubtedly by shorter life expectancies.

It will be noted that the proportion of total population below 15 years of age in the Netherlands is approximately the same as that in the Netherlands East Indies. Since the birth rate in the Netherlands East Indies is approximately twice that in the Netherlands, these essentially identical ratios can result only because very high infant death rates exist in the Indies.

BIRTH RATES IN CERTAIN COUNTRIES

Birth rates are universally dependent upon a variety of factors. The general use of young unskilled labor and the relatively low cost

of rearing families make high birth rates usual in an agricultural economy. Generally low socioeconomic levels, with inferior educational standards, poverty, and child marriage, are conducive to high birth rates. Laws relating to child labor and infanticide affect birth rate

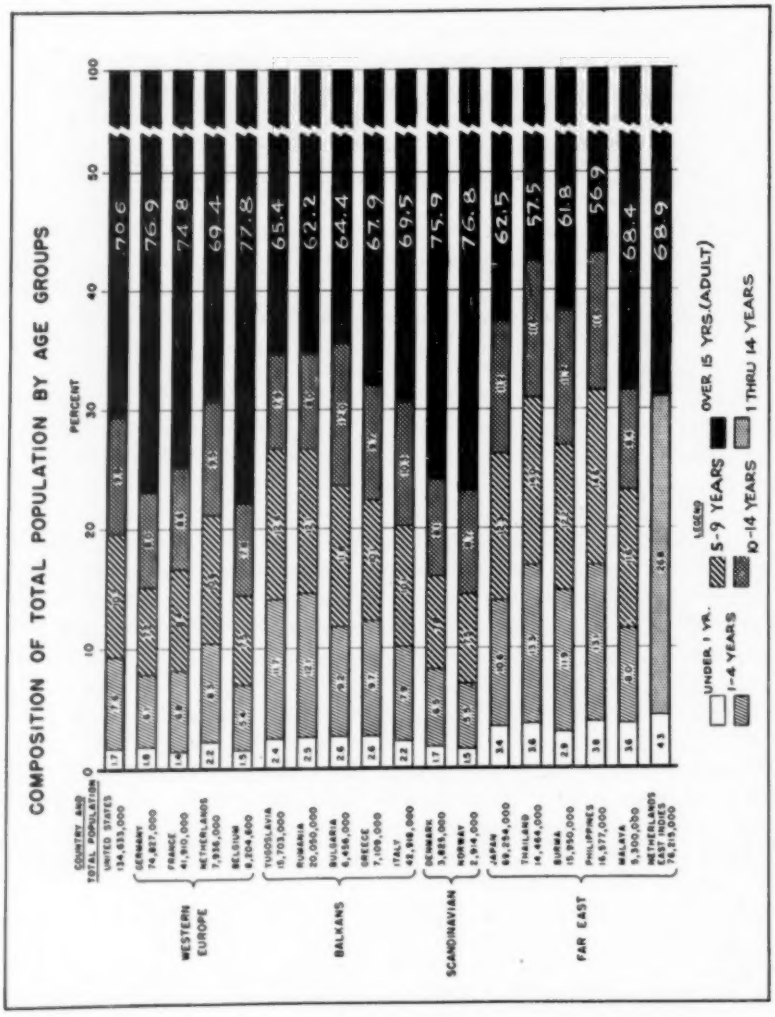

Fig. 1.

trends; certain religious restrictions, as those regarding birth control, are also modifying factors. Enumeration and discussion of all the factors influencing birth rates or the complicated interplay of such factors will not be attempted. Fig. 2 illustrates the comparative birth rates of

certain countries in North America, Western Europe, the Balkans, Scandinavia, and the Far East.

Comment.—Birth rates for Far Eastern countries are generally high; the reliability of the rate indicated for Indo-China is doubtful. Vital

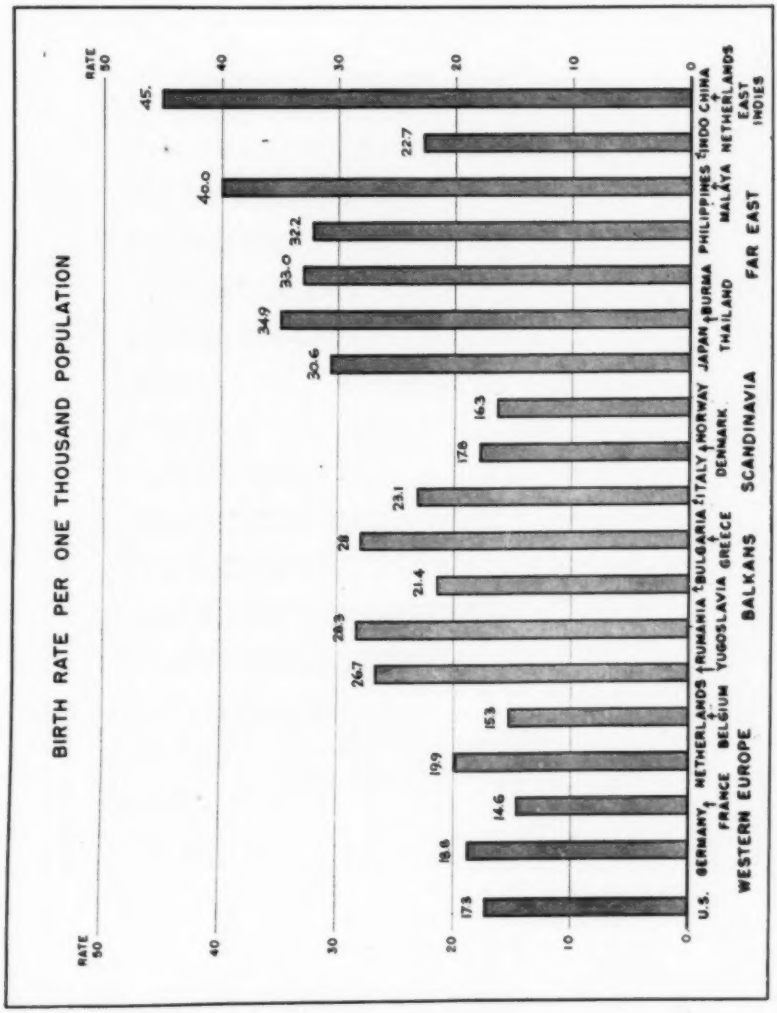

FIG. 2.

statistics pertaining to Indo-China were meager and certain data were entirely lacking. In Europe, birth rates are highest in the Balkan countries and lowest in France and Belgium. Birth rate in the United States is comparable to that of the Scandinavian countries.

INFANT MORTALITY IN CERTAIN COUNTRIES

Infant mortality rates will be favorably influenced by such factors as modernism in concepts of infant feeding, general knowledge of proper sanitation in food storage and preparation, adequate facilities and com-

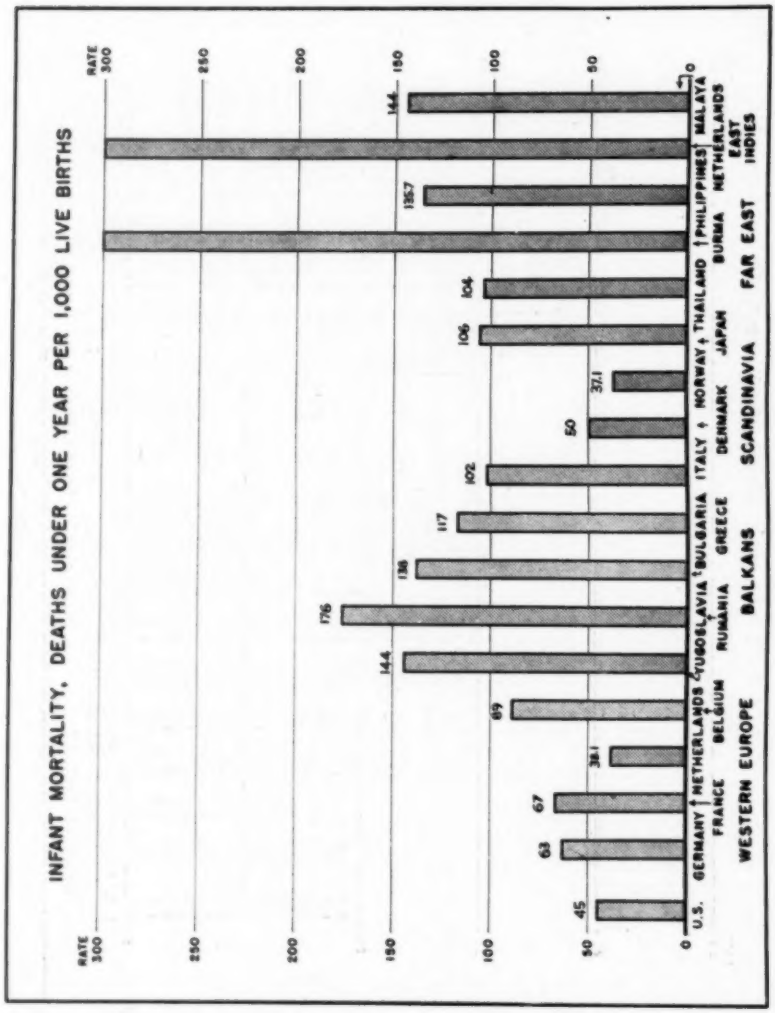

Fig. 3.

petent personnel for medical care, high levels of immunization for certain communicable diseases, and low incidence of infectious diseases with high morbidity rates for infants. Mortality rates will be high when the converse is true. The levels of these and certain other factors in-

fluencing infant mortality rate are variable in different geographic locations and countries; consequently considerable variation in infant mortality rates is to be expected. Fig. 3 indicates prewar infant mortality rates in certain countries; the rate indicated for each country is the most recent available (1938-1939).

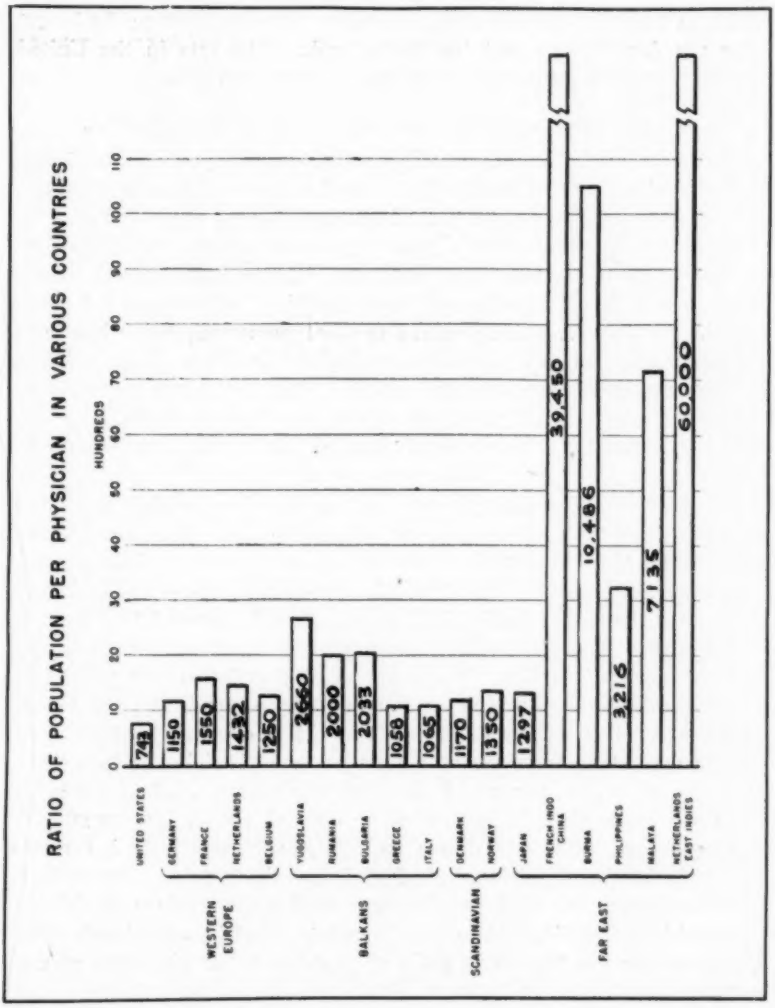

Fig. 4.

Comment.—Burma and the Netherlands East Indies have the highest infant death rates recorded in this study; rates in both countries exceed approximately two to three times those for the other included Far Eastern areas. Similar data for Indo-China were not available.

Although the causes of infant deaths in various countries have not been included herein, the importance of beriberi in parts of the Far East deserves mention. In Burma, the Netherlands East Indies, Japan, and the Philippines, infantile beriberi is a frequent cause of death in neonatal and later periods.[7, 8-10] In areas other than the Far East this disease is not important as a cause of infant mortality. The Balkan countries have the highest infant mortality rates in Europe; the lowest rates are for Norway and the Netherlands. The rate in the United States is greater than in these last two European countries.

RATIO OF POPULATION PER PHYSICIAN IN CERTAIN COUNTRIES

Within certain limits the ratio of population per physician is an index to the level of general health that may be expected in a population. Standards of medical education and care and certain other factors will, however, modify conclusions drawn from such ratios. In portions of the Far East there are large numbers of so-called "second class" physicians, individuals without formal training in recognized medical schools. Moreover, among native medical personnel, there has been little specialization in the pediatric and obstetric fields. Maternal and child care programs are frequently inadequate and at times nonexistent; obstetrics is a function relegated chiefly to midwives in many areas. Fig. 4 indicates the ratio of population per physician in various countries.

Comment.—The ratio of population per physician is high in all the Far Eastern countries; the highest ratios recorded occur for French Indo-China, the Netherlands East Indies, and Burma. Data of this type were not available for Thailand. Yugoslavia, Rumania, and Bulgaria have the highest ratios in Europe. It will be noted that in general a close parallelism exists for most countries as regards infant mortality rates (see Fig. 3) and ratios of population per physician. The highest infant mortality rates occur where physicians are fewest as compared to numbers of population. It is obvious, however, that factors other than numbers of population per physician influence the mortality rate; in Norway and Denmark, for example, infant mortality rates are lower than in certain other countries with less population per physician. Moreover, Japan and Italy, with relatively low ratios of population per physician, have high infant death rates. An analysis of these exceptions will not be attempted since various modifying geographic, economic, and sociologic factors must be considered. The United States has the lowest ratio of population per physician of any country.

CONCLUSIONS

Certain vital statistics and other data pertaining to children and child health have been reviewed. Knowledge of the composition of a population as to age groups, together with information pertaining to

disease incidence, provides a basis for planning types and quantities of biologicals, medicines, and medical supplies needed for immunization and treatment of infants and children. Moreover, information relative to numbers of children and birth and infant mortality rates are an index to the nature and extent of the health problems in an area. Knowledge derived from these data facilitates planning the development and re-establishment of adequate programs of nutrition and maternal and child care. Information regarding availability of trained medical personnel and facilities for treatment of the sick in each country is essential in public health planning; such data will indicate whether additional specialists and special facilities are needed for care of children. It is believed that formulation of adequate relief plans for infants and children in the postwar period will be facilitated by those data which reflect the prewar health status and problems in younger age groups.

REFERENCES

1. Notestein, F. W., and Others: The Future Population of Europe and the Soviet Union, Geneva, 1944, League of Nations.
2. Statistical Yearbook of the League of Nations 1939-1940, Geneva, 1940.
3. United States Dept. of Commerce, Bureau of Census: Vital Statistics Rates in the United States, 1900-1940, Washington, D. C., 1943, United States Government Printing Office.
4. Census of the Philippines, 1939, vol. 2, Manila, 1941.
5. Netherlands Indies, Dept. Economic Affairs, Central Bureau of Statistics: Statistical Abstracts of the Netherlands Indies 1940, Batavia.
6. Thai Government: Statistical Yearbook, Bangkok, 1939.
7. Medical Intelligence Division, The Preventive Medicine Service, Office of The Surgeon General, Washington, D. C.
8. Philippine Islands: Annual Report of the Bureau of Health, Bureau of Printing, Manila, 1939.
9. Résumé Statistique De L'Empire du Japon, Tokyo, 1935.
10. de Haas, J. H.: Geneesk. tijdschr. v. Nederl-Indië **79**: 707, 1939.

CHRONIC STRIDOR IN EARLY LIFE DUE TO PERSISTENT RIGHT AORTIC ARCH

Report of Two Cases

Harold K. Faber, M.D., John W. Hope, M.D., and
Francis L. Robinson, M.D.
San Francisco, Calif.

CHRONIC stridor is not uncommon in infancy and childhood and is due to a variety of causes. That it may be due to persistent right aortic arch is a fact of which physicians are not generally aware and which is rarely, if ever, mentioned in discussions of stridor in textbooks of pediatrics and rhinolaryngology, or even in papers on stridor, such as those of Kennedy and New,[1] and Bowman and Jackson.[2] On the other hand, many of the case reports of persistent right aortic arch mention stridor as a symptom, but more often they stress dysphagia (the so-called dysphagia lusoria) as a characteristic clinical manifestation, particularly in adults. In infants and children, however, noisy breathing appears to be much more common and dysphagia, while sometimes present, is less frequent and marked.

Assmann[3] first made the diagnosis during life. Since the publication of his paper in 1924 and of Arkin's[4] in 1926, the x-ray characteristics have been more generally recognized and the diagnosis more frequently made in living subjects, mainly, however, in adults. Garland,[5] who reviewed the literature in 1938, stated that of the approximately 113 cases on record only about thirteen were diagnosed during life. Pediatric attention to the malformation was attracted by the excellent report and review by Blackford, Davenport, and Bayley[6] in 1932, and more recently by Wolman.[7] Herbut and Smith in 1943[8] stated that only nine cases had been reported in infants and added another of their own. We find only four[6, 9, 10, 11] that were diagnosed during life, all of them in the course of investigation for other diseases and none of them suspected on the basis of stridor, the point which we wish to emphasize in this paper.

Within a period of three years we have observed two cases, both of which came to our attention because of noisy breathing.

CASE REPORTS

Case 1.—J. E., white male infant, was admitted to Stanford University Hospital March 1, 1940, at the age of 2 months because of noisy breathing which had been present from birth.

He was born at term, weighing 5 pounds, 12 ounces. While no cyanosis occurred, from birth the respirations were noisy, especially when he was awake. At 3 weeks an anomaly of the larynx was suspected; an x-ray picture was taken, which suggested enlarged thymus.

From the Department of Pediatrics, Stanford University School of Medicine.

Gavage was employed for the first three weeks because of respiratory trouble while feeding. During the two weeks before admission, breathing had become noisier.

On examination, there was no sign of obstruction of the airways, but each inspiration ended with a grunting sound. The noise was found to be more conspicuous when the child was awake and crying. The baby was in good condition and no physical abnormalities were noted excepting a left indirect inguinal hernia. Direct laryngoscopy showed the larynx to be somewhat hyperemic but otherwise normal.

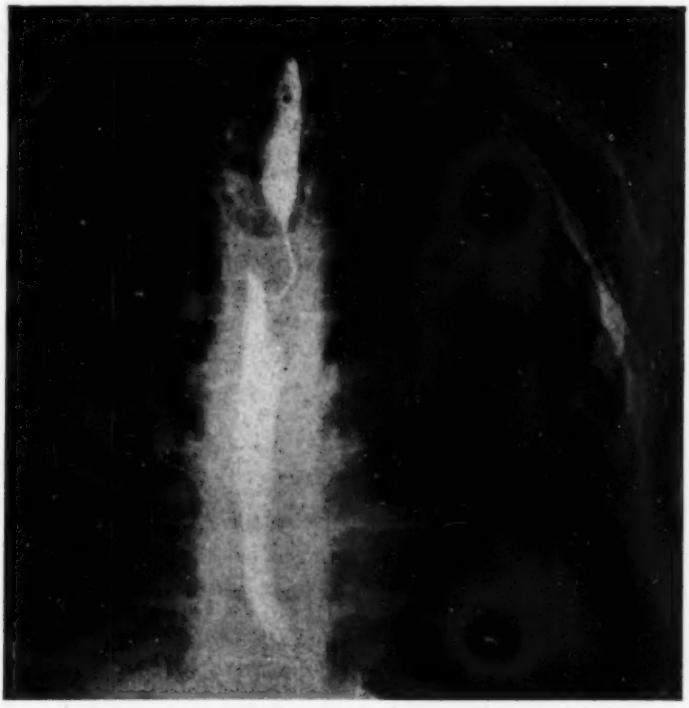

Fig. 1. (Case 1).—J. E. Anteroposterior view, with barium in esophagus, showing oblique filling defect opposite fourth and fifth thoracic vertebrae.

The laboratory data showed a mild anemia (red blood cells, 3,660,000; hemoglobin, 67 per cent Sahli). Urine, blood Wassermann, sedimentation rate, and tuberculin test were negative. No x-ray study was made at this time.

The baby was dismissed with the diagnosis of congenital stridor of unknown etiology.

About June 14, 1940, he had a cold, suddenly turned blue, became very dyspneic and was taken to another hospital where under steam inhalation he improved. Here he was thought to have an enlarged thymus, for which x-ray therapy was given. Some retraction of the suprasternal notch was observed at this time.

In March, 1941, a letter from his private physician stated that the child had a chronic cough and usually vomited once a day. A recent x-ray film had shown a "tumor mass" occupying one-third of the thoracic cavity in the midline. At our suggestion he was again brought to Stanford University Hospital on March 11, 1941.

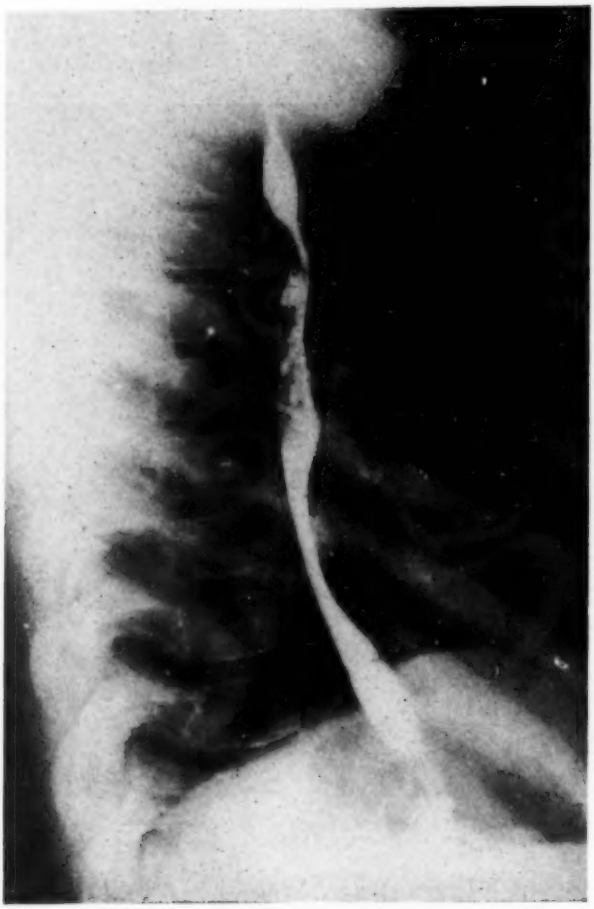

Fig. 2. (Case 1).—J. E. Lateral view. The filling defect shows the esophagus pushed forward. Behind it a faint rounded density, presumably the aorta, can be seen.

At this time, while his general condition was good, there was more respiratory difficulty than before, both inspiratory and expiratory. The lower ribs and suprasternal notch were retracted during inspiration. The stridor continued during sleep. There was some dullness over the upper sternum. Loud rhonchi were audible throughout the chest. No cardiac abnormalities were noted. The hernia had disappeared. Blood count, urine, Wassermann, and tuberculin tests were again negative.

Under the fluoroscope, an upper anterior mediastinal shadow was seen at the right of the spine reaching up to the right sternoclavicular joint; definite pulsation was repeatedly observed in it. No aortic knob could be seen at the left of the spine. Barium was then given orally and pictures taken (Figs. 1 and 2). These showed a deformity and filling defect in the esophagus at the level of the fourth and fifth thoracic vertebrae. Above the defect the esophagus was displaced slightly to the left and below it, slightly to the right. In the lateral view it was displaced forward. The presence of a bulge in the upper right portion of the great vessel shadow above the heart, and the absence of the aortic knob on the left gave the characteristic outline of right aortic arch (See Blackford, Davenport, and Bayley's case[6]).

A series of angiocardiograms after intravenous 70 per cent diodrast was made, the pictures being taken approximately three seconds apart. Two of these were taken at exactly the same period of respiration but at a slightly different period of the heart cycle. Superimposed tracings (Fig. 3) show expansion of the upper right vessel shadow.

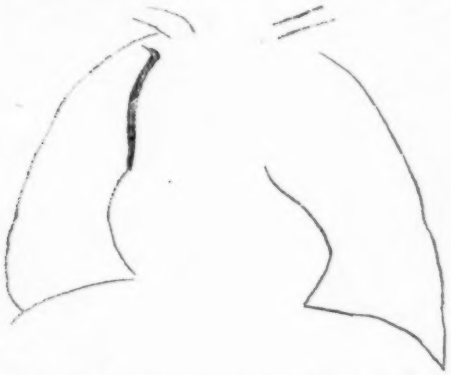

Fig. 3. (Case 1).—J. E. Superimposed tracings from two angiocardiograms after intravenous diodrast. The shaded area is the only difference between the two pictures and demonstrates pulsation of the right aorta.

Another laryngoscopy was done and esophagoscopy was also included. The laryngeal structures were quite normal. In the esophagus, about 1.5 cm. below the cricopharyngeus, a constriction was seen in the right posterior aspect; pulsation could not be definitely made out.

A recent review of the films by Dr. Frank Windholz of our Division of Radiology revealed two points hitherto overlooked. The widened right mediastinal shadow could, on close inspection, be followed downward into a right paravertebral shadow having the usual appearance of the descending aorta (Fig. 4); and an additional indentation was found in the barium-filled esophagus which was interpreted as due to a retro-esophageal left subclavian artery.

The complete diagnosis therefore in this case was: persistent right aortic arch; right-sided descending thoracic aorta; anomalous retro-esophageal subclavian artery.

The child has been repeatedly seen since then, the last time on June 21, 1944. The noisy breathing has continued and, especially when eating, he has attacks of severe cyanosis. Eating is slow and difficult.

Colds, which have become increasingly frequent, have made the respiratory difficulty worse and cause severe, exhausting bouts of coughing. The heart, however, has not become enlarged and exercise tolerance is good. The blood pressure on June 21 was 94/68. The last fluoroscopic examination on May 29, 1944 again showed the same outlines of the cardiovascular shadow and the same filling defects of the esophagus as before.

Fig. 4 (Case 1).—J. E. Anteroposterior view. Note the absence of vessel shadows on the left and their prominence on the right. The right descending aortic shadow can be followed downward to about the level of the eighth thoracic vertebra, gradually moving toward the left.

CASE 2.—T. J., white male, was admitted to Stanford University Hospital on May 12, 1943, at the age of 2½ years with the complaint of recurrent attacks of difficult breathing for two years.

At birth the baby was briefly cyanotic. At 4½ months he was said to have had pneumonia and inspiratory stridor was then first noticed. During another attack of pneumonia at 6 months, the stridor was much worse and an x-ray film at that time was said to have shown narrowing of the trachea. Since then he has had frequent attacks of inspiratory and expiratory stridor lasting two or three days and said to be brought on by exertion. They have not been accompanied by cyanosis. It was stated that he has had difficulty in swallowing solid foods.

The child, who was well nourished and developed, was observed to breathe with inspiratory and expiratory stridor but this was not severe enough to produce either cyanosis or retraction of the suprasternal notch. No other abnormalities were noted on physical examination. Routine laboratory tests were negative.

The x-ray films were reviewed by Dr. Windholz, whose report is herewith summarized.

Both lung fields were of normal translucency. The upper mediastinal shadow on the right was wider than on the left by about 3 mm. The heart was in normal position. The right auricular shadow was slightly bulging; other parts of the cardiac silhouette revealed no abnormalities.

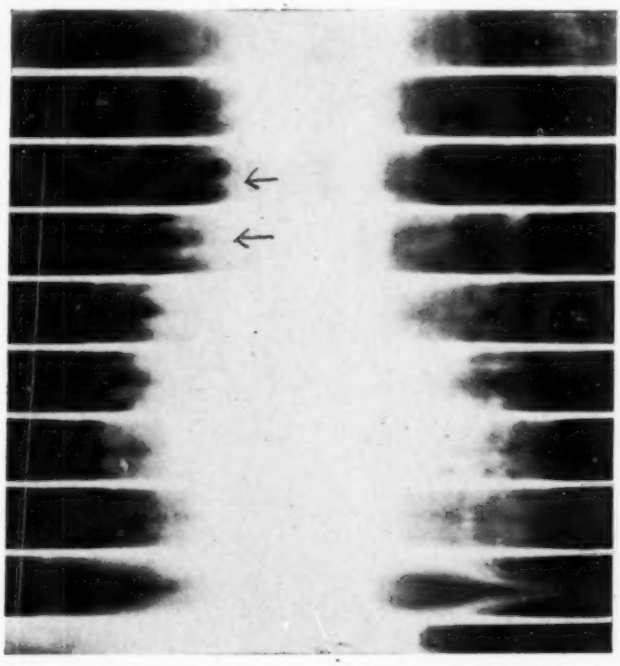

Fig. 5 (Case 2).—T. C. Kymogram. Opposite the arrows, which point to the right, deep waves of pulsation of the right aorta are seen while none is visible on the corresponding area of the left side.

The area of the pulmonic arch was full. No aortic knob was visualized on either side. However, some of the films revealed a slight bulging of the widened right upper mediastinum.

Kymographic studies showed vigorous pulsations in the right upper mediastinum (Fig. 5). The pulsations were almost synchronous with those of the left ventricle and the configuration of the waves corresponded with pulsation. No pulsations were seen in the left mediastinum or in the trachea. The esophagus revealed remarkable changes. (Figs. 6 and 7). It was compressed from the right side about one inch below the sternal notch. It also was displaced toward the left and anteriorly. Density behind the displaced esophagus revealed outlines of the aortic arch.

Laminagraphic studies showed that the trachea was compressed slightly above the bifurcation on the right side and the angulation of the bifurcation was reversed.

Conclusion.—The diagnosis was persistent right aortic arch displacing esophagus and trachea anteriorly and to the left.

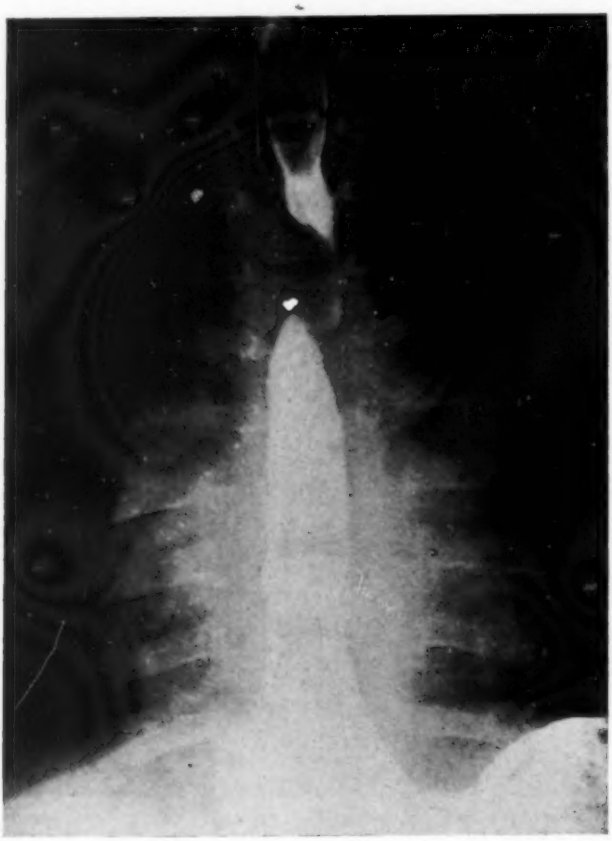

Fig. 6 (Case 2).—T. C. Anteroposterior view with barium in the esophagus showing the typical oblique filling defect.

DISCUSSION

For a discussion of the embryology and comparative anatomy of anomalies of the aorta the reader is referred to Dr. Maude Abbott's Atlas of Congenital Cardiac Disease[12] and to the papers of Arkin[4, 13] and of Blackford, Davenport, and Bayley.[6] It is necessary here only to say that the malformation consists essentially of persistence of the embryonic right fourth aortic arch together with a variety of anomalies of the left aorta, the arteries of the neck (especially the subclavian) and sometimes of the ductus arteriosus or ligamentum arteriosum. The left

aortic arch may be partly or wholly suppressed, or it may fully persist (double arch). The common factor in the various cases and the one which produces the clinical manifestations of dysphagia and stridor as well as the characteristic filling defect in the esophagus is compression of the esophagus by the right arch as it passes behind the esophagus in its course toward the descending aorta. This is usually at the level of the bifurcation of the trachea, but in some instances (as in the case of Snelling and Erb[11] and in our Case 1) it descends somewhat lower

Fig. 7 (Case 2).—T. C. Lateral view showing the filling defect with forward displacement of the esophagus.

on the right before crossing over. Occasionally, the right and left aortas are connected in front of the trachea as well as behind it, forming a vascular ring around both trachea and esophagus. In front the right aorta passes over the right main bronchus at the side of the trachea and may compress the latter, as in our Case 2.

In some instances no symptoms occur. Difficulty in swallowing is common and was present in both our cases. More conspicuous in children is noisy breathing, accentuated during exertion or during feeding, which may at times be severe enough to cause retraction of the suprasternal notch, rib cage, and epigastrium, cyanosis, and even, as in the case of Schall and Johnson,[14] extreme extension of the head. During sleep the stridor tends to diminish or disappear. Respiratory infections are likely to cause exacerbations of the obstructive trouble.

During life the diagnosis is entirely dependent upon x-ray examination but, since special techniques are required, cases will almost certainly be missed unless the clinician or radiologist suspects and looks specifically for the anomaly. Our experience leads us to the belief that suspicion should be aroused and suitable x-ray study made of every case of stridor in infancy and early childhood not due to obvious causes, such as infection, foreign body, or gross laryngeal malformation.

The most characteristic roentgenographic features are the anterior displacement of the esophagus at the level of the bifurcation of the trachea (lateral view) and the rounded filling defect of the esophagus which, in the anterior view, is displaced to the left. Under the fluoroscope, pulsation of the margins of the defect is visible. As Arkin[4, 13] pointed out, the knob of the right aorta can be seen behind the esophagus as a round mass, while the normal left aortic knob is absent. In the anterior view, in some cases at least (as in our case and in Blackford's), the right aortic arch stands out boldly at the right of the vertebral column above the heart shadow as a rounded prominence, which might easily be mistaken for enlarged right lobe of the thymus. Arkin made a particular point of the value of the first, or right anterior oblique, position in x-ray examination, which best brings out the position of the aorta behind the esophagus, the forward displacement of the esophagus and trachea and the appearance of the aortic knob under the sternal end of the right clavicle separated from the heart shadow by a characteristic light band representing the trachea and right main bronchus. Careful inspection under the fluoroscope will usually reveal pulsation of the prominence in the right upper mediastinal shadow and at the margins of the filling defect in the esophagus. Pulsation may also be seen by bronchoscopy or esophagoscopy and may be demonstrated by kymograms, or by angiograms with opaque substances in the blood stream (as in our Case 1). The latter method is, however, too cumbersome and uncertain to be of much practical value. The best method is kymography, as demonstrated by Arana and Aguirre[9] and in our Case 2, which gives uncontrovertible, objective evidence of pulsation in the margin of the upper right mediastinal shadow. We suggest that whenever available this method should be routinely used in suspected cases.

Ordinary physical examination is of little assistance. In uncomplicated cases there is no murmur. Arkin stated that the second aortic sound is heard best over the sternal end of the right clavicle. Dullness may be elicited to the right of the upper sternum.

In the rare cases of double aortic arch with total persistence of the left arch, the esophagus is not pushed to the left but is uniformly constricted. A case of this kind was reported by Snelling and Erb.[11]

Persistent right arch is to be differentiated from mediastinal tumor (for which a patient in Garland's[5] series was operated upon), aneurysm of the aorta and, especially in infants, enlargement of the thymus. The

roentgenological criteria previously described adequately distinguish right arch from these. *Barium in the esophagus is essential.* In the case of infants and small children, thymic hyperplasia is particularly apt to be diagnosed from a broad upper mediastinal shadow associated with a history of stridor. We are confident that persistent right arch has been the correct diagnosis in many cases of this sort and has been overlooked because it was not taken into consideration. This error, we suspect, is particularly apt to occur when the upper mediastinal shadow is unilateral and on the right side. In our opinion the diagnosis of thymic stridor, proved cases of which are certainly rare, should never be accepted until persistent right arch has been definitely excluded.

The prognosis cannot be stated in quantitative terms since most cases have not been recognized during life. Some of the patients live in good health, free of symptoms, even to advanced age. Blackford, Davenport, and Bayley[6] cited two reported instances in which death occurred at 78 and 87 years, respectively. The great danger to children with stridor is respiratory infection and many of the deaths have been caused by bronchopneumonia. Every effort should be made to shield them from such infections. Treatment of these complications should be early and adequate. Oxygen should be on hand.

SUMMARY

1. Stridor was the presenting symptom in two cases of persistent right aortic arch discoverd in early life and led to the appropriate x-ray investigation which established the diagnosis.

2. In congenital or chronic stridor not due to obvious causes, persistent right aortic arch should always be considered and investigated. The diagnosis of enlarged thymus and "thymic stridor," based on a broad shadow in the upper mediastinum, should not be accepted until persistent right arch has been excluded.

REFERENCES

1. Kennedy, L. J., and New, G. B.: J. A. M. A. **96**: 1286, 1931.
2. Bowman, J. E., and Jackson, C. L.: J. PEDIAT. **15**: 476, 1939.
3. Assmann, H.: Die hohe Rechtslage der Aorta, Klinische Röntgendiagnostik der inneren Erkrankungen, ed. 3, Leipzig, 1924, F. C. W. Vogel, 103 (cited by Blackford et al.).
4. Arkin, A.: Wien. Arch. f. inn. Med. **12**: 385, 1926.
5. Garland, L. H.: Am. J. Roentgenol. **39**: 713, 1938.
6. Blackford, L. M., Davenport, T. F., and Bayley, R. H.: Am. J. Dis. Child. **44**: 823, 1932.
7. Wolman, I. J. J. PEDIAT. **14**: 527, 1939.
8. Herbut, P. A., and Smith, T. T.: Arch. Otolaryngol. **37**: 558, 1943.
9. Arana, M. R., and Aguirre, R. S.: Arch. argentin. d pediat. **14**: 331, 1940.
10. Metzger, H. N., and Ostrum, H.: Am. J. Digest. Dis. & Nutrition **6**: 32, 1939.
11. Snelling, C. E., and Erb, I. H.: Arch. Dis. Childhood **8**: 401, 1933.
12. Abbott, M. E.: Atlas of Congenital Cardiac Disease, Am. Heart Assoc., New York, 1936.
13. Arkin, A.: Am. Heart J. **11**: 444, 1936.
14. Schall, L. A., and Johnson, L. G.: Ann. Otol., Rhin. & Laryng. **49**: 1055, 1940.

TUBERCULOUS PLEURISY WITH EFFUSION IN INFANCY

JANET B. HARDY, M.D., BALTIMORE, MD., AND EDWIN L. KENDIG, JR., M.D.
RICHMOND, VA.

THE records of the Tuberculosis Clinic of the Harriet Lane Home provided the material for this study. The requirements for admission to this clinic are that the child shall be under 2 years of age, and already infected with tuberculosis, or a close contact with sputum positive tuberculosis in a member of the household. In this study only those patients already infected with tuberculosis were considered. Those children who were lost sight of within two years of their admission to the Clinic were excluded from the study. This material covers the period from 1928 to 1944 and constitutes the first part of a study dealing with tuberculous pleurisy with effusion in children.

The criteria used for diagnosis were as follows:

1. The demonstration of tubercle bacilli by culture or guinea pig inoculation of the pleural fluid provided positive proof of the diagnosis in slightly less than one-half of this series.

2. Calcification in the pleura after disappearance of the fluid completed the diagnosis in one instance.

3. In the rest, a positive tuberculin test, the demonstration of pleurisy with effusion, and the subsequent course of the disease were considered sufficient (See case reports and Figs. 1 to 9.)

In none of these patients so diagnosed was there evidence of any disease which might be construed to be due to some organism other than the tubercle bacillus. The records of two patients were discarded from the study. Although they were tuberculin positive and had probable mediastinal tuberculosis by x-ray, the pneumonic infiltrations which coincided with the pleural effusion were short-lived and were accompanied by high fever. No thoracentesis was done and while no pyogenic organisms were isolated from the nasopharynx, and the cases were at the time diagnosed as tuberculous pleural effusions, it was felt that their doubtful character made them unfit for inclusion in this study. In retrospect, a diagnosis of pneumonia with serous effusion seems more probable.

Of 393 children infected with tuberculosis under the age of 2 years, thirteen cases of tuberculous pleurisy with effusion occurred. This represents an incidence of 3.3 per cent and seems to indicate that pleurisy with effusion is not a rarity. It also seems worthy of mention that a fibrinous pleurisy demonstrable by x-ray was present in thirty-two other children in this series.

Age at Which Pleural Effusion Occurred.—The age incidence varied from 10 to 28 months. Only one of the thirteen patients was older than 20 months and she had demonstrable tuberculous infection before the age of 2 years; this child had a longer history of preceding tuberculous infection than did the others.

From the Department of Pediatrics, Johns Hopkins University School of Medicine and the Harriet Lane Home, Johns Hopkins Hospital, Baltimore, Md.

This study was aided in part by a grant from the Commonwealth Fund.

TABLE I

AGE DISTRIBUTION

AGE IN MONTHS	NUMBER OF CASES
10 to 15	4
16 to 20	8
21 to 30	1

Incidence in Relation to Sex and Color.—The sex distribution of six males and seven females is of no significance.

Of 261 Negro children in this study eleven, or 4.2 per cent, developed pleurisy with effusion, while only two, or 1.5 per cent, of the 132 white children developed this condition. This conforms with the work of Brailey,[1, 2, 3] who demonstrated that the percentage of severe pulmonary lesions in infected Negro children is about twice that found in infected white children.

TABLE II

COLOR OF DISTRIBUTION

	NUMBER INFECTED	NUMBER WITH PLEURAL EFFUSION
Negro	261	11
White	132	2
Total	393	13

Nature of the Underlying Tuberculous Process. Unlike the conditions obtaining in older children and adults, in every patient in this series an underlying tuberculous lesion was demonstrable by x-ray. These underlying lesions may be divided into two groups. There were seven patients with only a primary tuberculous complex. All of these made an uneventful recovery. The six other patients had mediastinal tuberculosis complicated by tuberculous pneumonia; two of these developed cavitation and both received pneumothorax therapy. There seemed to be a definite relationship between the pneumothorax therapy and the appearance of pleural fluid in only one of these and this patient had tubercle bacilli in her pleural fluid. In the other patient fluid appeared before the pneumothorax was instituted. This fluid disappeared, however, only to reappear when pneumothorax therapy had been in use about three months. At autopsy, nine months later, a tuberculous empyema was found on the side of the pneumothorax and a serous pleural effusion on the other.

Duration of Tuberculous Process Before Pleurisy Became Manifest.—Since all the children in this series were under 29 months of age when the pleurisy developed, it is obvious that the tuberculous process could not have been of long duration. In the ten cases in which it could be determined the duration varied from one to six months, with seven cases of three months or less.

Duration of Pleurisy With Effusion.—The duration of the pleural effusion varied between one and twelve months with the majority lasting less than six months.

TABLE III

DURATION OF PROCESS BEFORE MANIFESTATION OF PLEURISY

TIME IN MONTHS	NUMBER OF CASES
1	1
2	2
3	4
4	1
5	1
6	1
Not known, 3	

TABLE IV

DURATION OF PLEURAL EFFUSION

TIME IN MONTHS	NUMBER OF CASES
1	3
2	2
3	1
4	1
6	1
7	1
9	1
10	1
11	1
12	1
Not known, 1	

One patient had a recurrence of pleural effusion.

Outcome.—Of the thirteen patients in this series, eight recovered with healing and calcification of the primary complex. Two patients later developed the adult, or reinfection, type of tuberculosis and one of these died with renal tuberculosis fourteen years later. Three other patients died of tuberculous meningitis, complicating severe pulmonary lesions, one of the miliary, and two of the pneumonic type. All four deaths occurred in Negro patients.

History of Exposure.—In eleven cases in this series, nine Negro and two white, there was definite history of exposure to sputum positive tuberculosis. Four children were exposed to a tuberculous father, three to a tuberculous mother, three to close relatives who spent considerable time with the children as visitors, and one to a close friend who lived near by. In the remaining two children the only history of exposure obtainable was to siblings with mediastinal tuberculosis. With reference to these it seems more than likely that the infected children in the household all received their infection from the same undiscovered, though carefully searched for, adult type of case.

DISCUSSION

It should be emphasized that this study deals only with infected infants and is in no way representative of the conditions which obtain in older children. Study of the literature suggests that under the age of 3 years pleurisy with effusion is a rarity.

In ninety-six consecutive cases of tuberculous serofibrinous pleurisy taken from the diagnostic files of the Harriet Lane Home, the average age at onset of the pleural effusion was 6½ years. These patients varied

from 7 months to 14 years of age. In the series of Wallgren and associates[4] 443 consecutive cases of serofibrinous pleurisy reported from the Gothenburg Children's Hospital in Sweden, there were no patients under 1 year, only two, between 1 and 2 years, and fifteen, between 2 and 3 years. Myers and Rollie[5] found fifty-eight cases of pleurisy of all types in 2,000 children studied at the Lymanhurst School for Tuberculosis. Among these there were no patients under 3 years of age. There are scattered reports through the literature[6, 7, 8, 9] of isolated cases occurring in infants, but these are not numerous. The youngest instance of pleurisy with effusion to come to our attention was a 3-month-old Negro female, seen by Dr. Margaret Smith, at Sydenham Hospital, Baltimore. This infant, who had been in contact with her mother who had sputum positive tuberculosis, had a pleural effusion coincident with acute miliary tuberculosis, from which she died at the age of 4 months.

The pleural effusion was found to occur early in the disease in each case. In those cases in which the duration of the tuberculous process prior to the manifestation of the pleurisy was known, it occurred within the first six months of the disease, and in the majority of the cases within the first three months. In the three other cases of tuberculous pleural effusion occurring in the clinic, but not included in the study as the children were infected when over 2 years of age (27 months, 30 months, and 7 years) the pleural effusion appeared in 1, 7, and 6 months, respectively, after infection.

As far as could be judged from this small series, the occurrence of serofibrinous pleurisy had no effect on the ultimate prognosis. As has been previously shown by other workers on pleurisy in older children and adults, the prognosis depends upon the severity of the accompanying tuberculous process.

SUMMARY

1. Of 393 children infected with tuberculosis under the age of 2 years, thirteen, or 3.3 per cent, developed pleurisy with effusion.

2. The incidence of pleural effusion in Negro children was 4.2 per cent, and in white children, 1.5 per cent.

3. The age incidence was from 10 to 28 months.

4. An underlying tuberculous process was demonstrated in each case.

5. The serofibrinous pleurisy occurred early in the course of the disease.

6. As far as could be determined, the occurrence of pleurisy with effusion was without effect on the ultimate prognosis.

CASE REPORTS

CASE 1.—M. T., a 20-month-old Negro girl, was admitted with fever 104° F. and signs of pneumonia over the left lower lobe. She had a history of illness of only three days' duration. Her only known contact was with childhood tuberculosis. She was found to have mediastinal tuberculosis and pleurisy with effusion. Tubercle bacilli were demon-

strated from the pleural fluid. The pleural fluid was demonstrable by x-ray for about two months. X-ray at 9 years of age showed the lungs to be clear.

CASE 2.—F. S., (Fig. 1*) 19-month-old Negro female, was first seen with fever 104° F. and signs of pneumonia over the right lung base. There was no history of illness prior to a few hours before admission. Tuberculous contacts were her mother, from whose home she was removed at the age of 2 weeks, and her foster mother. Enlargement of the mediastinal glands, pneumonia, and pleurisy with effusion were demonstrated by x-ray. Thoracentesis was productive of sterile green fluid (no guinea pig inoculation). The pleurisy with effusion persisted for ten months. At the age of 12 years, she developed reinfection tuberculosis and died two years later of renal failure.

CASE 3.—I. A., (Fig. 2) a white girl, slept with her tuberculous mother for the first seven months of life. At the age of 1 year she was seen in the dispensary because of a paroxysmal cough of two months' duration. X-ray revealed mediastinal tuberculosis and pleurisy with effusion; one month later the child was sent to a sanatorium. The next films taken there showed no sign of fluid. X-ray at the age of 6 years showed a calcified primary complex bilaterally.

CASE 4.—P. R., a Negro female, was exposed to her father who had sputum positive tuberculosis. At the age of 11 months she had tuberculous pneumonia with cavitation. Pneumothorax therapy was instituted. Five months later she was admitted to the hospital with history of malaise, vomiting, and fever of 104° F., greenish seropurulent fluid was withdrawn from the pleural cavity. Guinea pig inoculation was positive for tubercle bacilli. The pleural effusion persisted for about one year. She was then well until 10 years of age when she developed reinfection tuberculosis. After five months of sanatorium care she was ready for discharge.

CASE 5.—G. McC. (Figs. 3 and 4) a Negro boy, whose mother died of tuberculous meningitis and whose uncle had sputum positive tuberculosis, was diagnosed as having mediastinal tuberculosis and tuberculous pneumonia at 16 months of age. Two months later x-ray revealed an interlobar pleural effusion. No thoracentesis was done and the child was sent to a sanatorium. The duration of the pleurisy could not be determined as no lateral films were taken at the sanatorium. X-ray of his chest at 4 years of age showed a calcified primary complex on the right.

CASE 6.—M. R. (Fig. 5) a Negro girl, had measles at 15 months of age. Following this she developed a persistent cough, lost weight, and ran an intermittent fever. Her left ear drained persistently. She was admitted to the hospital three months later for mastoidectomy. At that time she was found to have severe mediastinal tuberculosis, and pleurisy with effusion; the latter lasted five weeks. The patient died of tuberculous meningitis and miliary tuberculosis a month later. The only known tuberculous contact was her sister who had mediastinal tuberculosis.

CASE 7.—M. G., a Negro boy, was exposed to a family friend who had sputum positive tuberculosis. The child was admitted to the hospital

*Figs. 1 to 9 are x-ray pictures of those patients in whom guinea pig inoculation was not positive for tubercle bacilli. These x-rays were chosen, where possible, to show the underlying tuberculous process as well as the presence of a pleural effusion and they do not in every case show the maximum amount of fluid which was present.

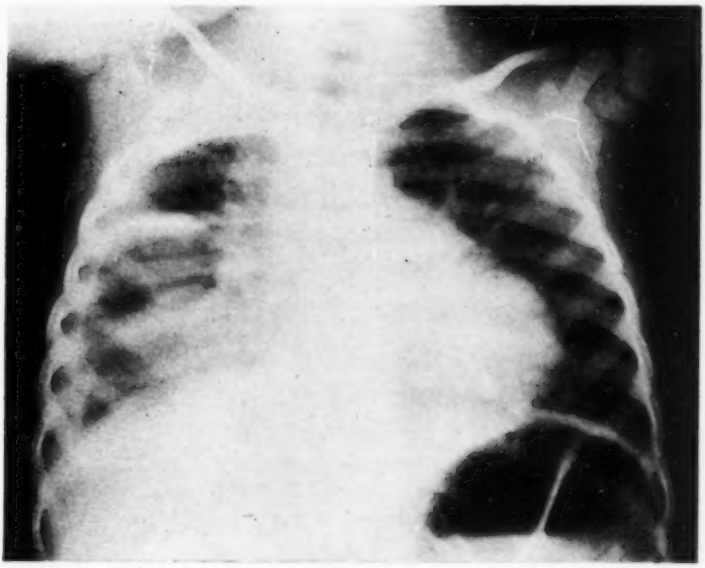

Fig. 1.—F. S., aged 20 months, mediastinal tuberculosis, tuberculous pneumonia, and pleurisy with effusion.

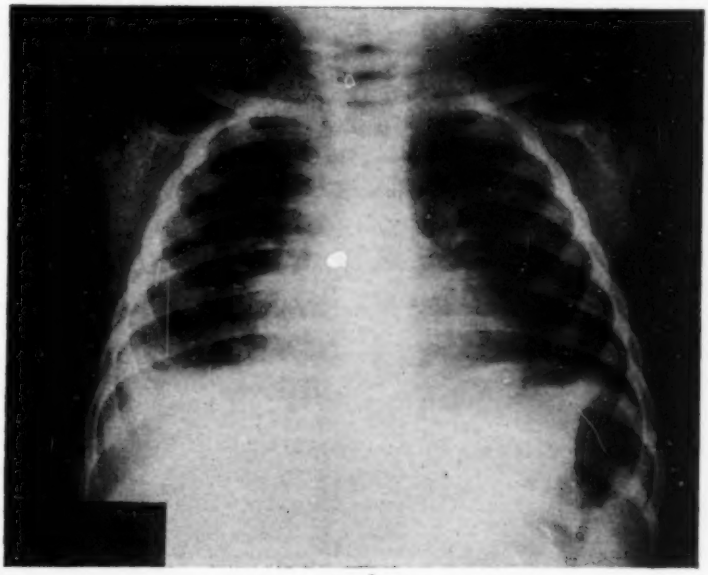

Fig. 2.—I. A., aged 12 months, bilateral mediastinal tuberculosis, serofibrinous pleurisy, right.

Fig. 3.—G. McC., aged 18 months, mediastinal tuberculosis and clouding over the right lower lobe.

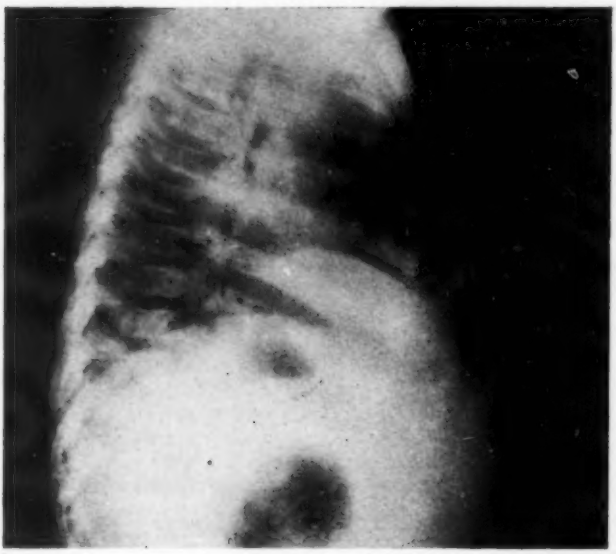

Fig. 4.—G. McC., aged 18 months, right lateral showing interlobar pleural effusion.

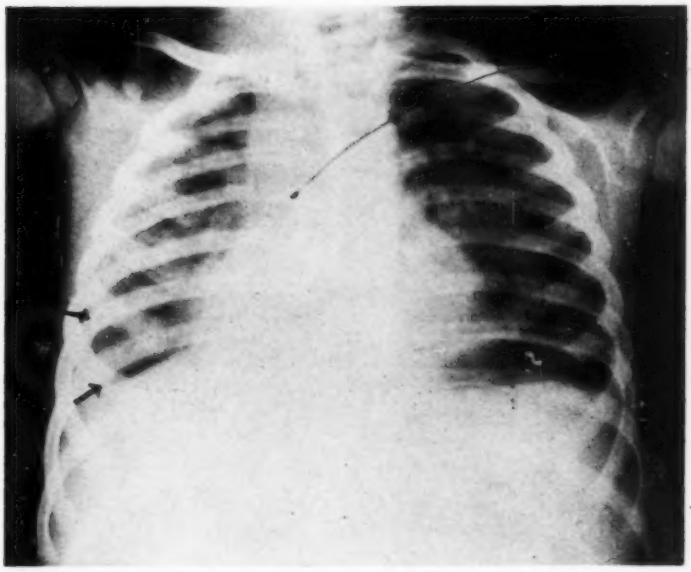

Fig. 5.—M. R., aged 18 months, mediastinal tuberculosis, serofibrinous pleurisy, right, and early miliary tuberculosis.

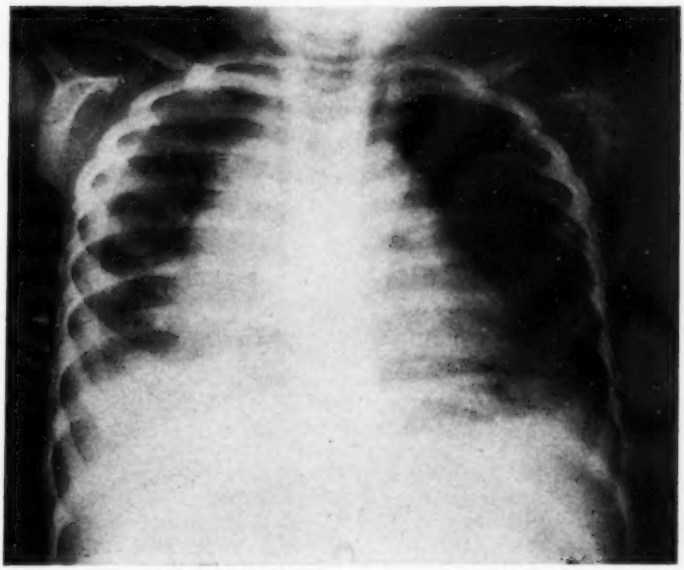

Fig. 6.—R. C., aged 12 months, mediastinal tuberculosis, tuberculous pneumonia, and pleural effusion.

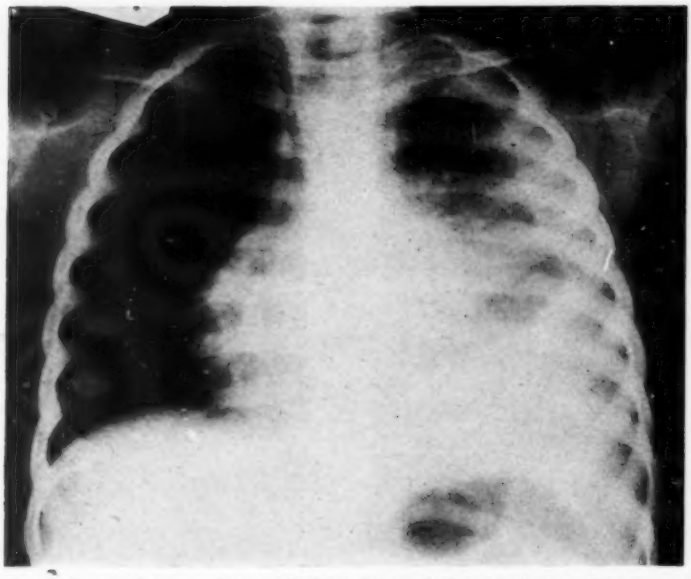

Fig. 7.—V. R., aged 22 months, mediastinal tuberculosis and pleural effusion on left.

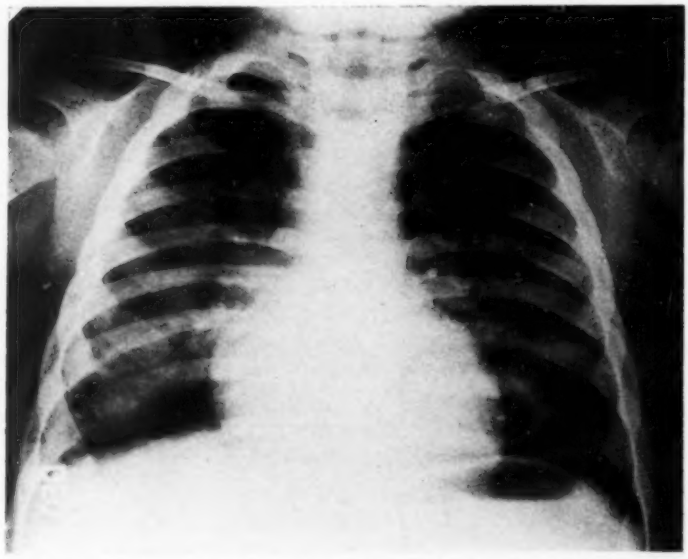

Fig. 8.—J. D., aged 17 months, mediastinal tuberculosis with pleural effusion on right.

at 18 months of age with history of fever, chronic cough, loss of weight and capricious appetite of three months' duration. On admission he had fever 102.4° F. and was found to have tuberculous pneumonia and pleurisy with effusion. Tubercle bacilli were demonstrated from the pleural fluid. His course was steadily downhill and he died of tuberculous meningitis three months later.

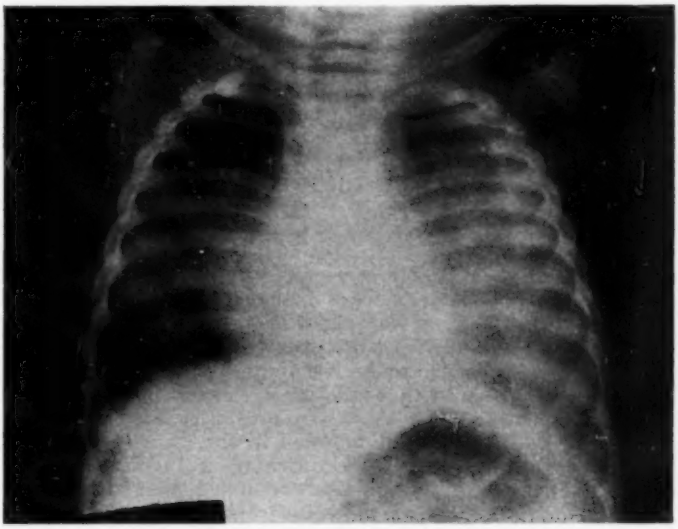

Fig. 9.—M. K., aged 10 months, mediastinal tuberculosis with pleural effusion on left.

CASE 8.—R. C. (Fig. 6) a Negro male, was exposed to his father who had pulmonary tuberculosis. At 10 months of age the child was found to have mediastinal tuberculosis. Two months later x-ray revealed tuberculous pneumonia and serofibrinous pleurisy. The pleural effusion lasted for about six months. When the child was 3 years of age he developed and recovered from an illness which clinically appeared to be tuberculous meningitis and tubercle bacilli were isolated from the spinal fluid on one occasion. X-ray at 14 years of age shows calcification in right lung.

CASE 9.—V. R. (Fig. 7) a Negro female, was exposed to her father, who had sputum positive tuberculosis and a pleural effusion. She was seen in the dispensary at 22 months of age and was found to have asymptomatic mediastinal tuberculosis. Two weeks later she was admitted to the hospital with temperature 104° F. and signs of massive pleural effusion on the left. Thoracentesis yielded straw-colored fluid with many lymphocytes. Guinea pig inoculation failed to demonstrate tubercle bacilli. X-ray showed mediastinal tuberculosis and pleural effusion. The fluid cleared slowly and was gone in eleven months. The mediastinal tuberculosis healed with calcification. X-ray at 15 years of age showed the lungs to be clear, with a calcium deposit at left hilum.

CASE 10.—R. H., a Negro girl, was exposed to her grandmother and aunt, both of whom had tuberculosis, when they visited her home. She had vague symptoms from 13 months of age. At 17 months she became ill with fever 103.4° F. and signs of pneumonia and pleural effusion on

right. She was found by x-ray to have a tuberculous pneumonia and interlobar pleural effusion. Guinea pig inoculation of the pleural fluid was positive. The pleural effusion was demonstrable by x-ray for seven months. The pneumonia cleared very slowly and eventually healed with massive calcification. At 6 years of age the lungs were clear except for massive parenchymal and mediastinal calcification on the right.

CASE 11.—J. D. (Fig. 8) a white boy, was exposed to his tuberculous mother from birth to 16 months of age. At 17 months he was found to be positive to 0.1 mg. tuberculin. X-ray showed a massive pleural effusion on the right. He had had no symptoms and was gaining weight. He was admitted to the hospital where the effusion showed signs of rapid clearing. After two weeks he was transferred to a sanatorium with the diagnosis of mediastinal tuberculosis. He made an uneventful recovery. X-ray of his chest was clear at 3 years of age.

CASE 12.—H. T., a Negro male, was exposed to an aunt who died of tuberculosis. At the age of 10 months he developed fever, anorexia, and weight loss. One month later there was x-ray evidence of mediastinal tuberculosis, tuberculous pneumonia in the right lower lobe and a small amount of pleural fluid at the right base. The tuberculous process cleared somewhat and the fluid disappeared. Four months later, however, the child was admitted to the hospital because of progression of the tuberculous pneumonia with cavitation. Pneumothorax therapy was instituted and continued for about 4 months. At this time he was discharged from the hospital and followed in the dispensary, where, one month later, he was found by x-ray to have pleural effusion on the right, which became massive. He was readmitted ten months later with tuberculous meningitis from which he died. At autopsy tubercle bacilli were recovered from the empyema on the right and there was a serous pleural effusion on the left, in addition to generalized tuberculosis.

CASE 13.—M. K. (Fig. 9) a Negro boy, became ill at 6 months of age with fever, a brassy cough, diarrhea, and failure to gain weight. He had been exposed to his father who had sputum positive tuberculosis. The child's tuberculin test was positive and he was admitted to the hospital for study. He was found to have mediastinal tuberculosis, congenital lues, and mild rickets. He improved during his hospital stay. At 10 months of age he was readmitted with history of acute illness of one week duration. He had fever of 102.6° F. and signs of a pleural effusion on the left. Thoracentesis yielded straw-colored fluid, with a differential count of 95 per cent lymphocytes. No tubercle bacilli were demonstrated from this fluid. After two months the pleural effusion disappeared. He made an uneventful recovery. At 14 years of age x-ray of his chest showed calcified primary foci in each lung.

REFERENCES

1. Brailey, M. E.: Milbank Memorial Fund Quarterly **15**: 1, 1937.
2. Brailey, M. E.: Am. Rev. Tuberc. **36**: 347, 1937.
3. Brailey, M. E.: Am. J. Pub. Health **33**: 343, 1943.
4. Wallgren, A., in Miller, J. A., and Wallgren, A.: Pulmonary Tuberculosis in Adults and Children, New York, 1939, Thomas Nelson & Sons, p. 162.
5. Myers, J. A., and Rollie, C. A.: Am. Rev. Tuberc. **11**: 398, 1925.
6. Heinila, H.: Duodecim **55**: 772, 1939.
7. Mazzeo, A.: Pediatria **40**: 26, 1932.
8. Delbecq, E.: Rev. de la tuberc. **5**: 215, 1939.
9. Girand, P., Poinso, R., Salmon, M., and Mockers: Bull. Soc. pédiat. de Paris **36**: 488, 1938.

PURULENT PAROTITIS IN THE NEWBORN

HEYWORTH N. SANFORD, M.D., AND IRENE SHMIGELSKY, M.D.
CHICAGO, ILL.

PURULENT parotitis, according to the number of reported instances, has been considered a rare occurrence in the newborn. Plewka[1] reviewed the existing literature in 1921 and collected fifty-one cases. Elterich[2] in 1922 added another instance and included two others appearing since Plewka's report. Since this time three other cases have been added; Baxter and MacDonald,[3] and Bloch and Pacella[4] (two cases). These with the five that we are now giving makes a total of sixty-two of these cases to be reported. Elterich's articles gives a full bibliography up to 1933, and this will not be repeated.

However, we believe that this condition is encountered in greater frequency than the number of reported cases would indicate. Almost every pediatrician who has had experience with newborn infants will mention having seen one or more instances of purulent parotitis over the course of years. They have either not bothered to report it, or are waiting for another case. Our purpose is to discuss a disease entity which we believe is seen frequently enough to warrant common knowledge of diagnosis and adequate treatment.

CASE HISTORIES

CASE 1.—A white male infant, weighing 5 pounds, was born normally to a mother whose Wassermann and Kahn tests were positive. The spleen was palpable and the roentgenograms revealed bands of decreased density across the ends of the long bones. The infant was given premature care, placed in an incubator and fed lactic acid/breast milk by gavage. Acetarsone, 0.05 Gm., was given by mouth daily.

The infant progressed well until the eighth day of life when the temperature rose to 103° F. and a swelling was noticed in the region of the right parotid gland. Examination of the mouth revealed redness about the opening of Stensen's duct, and pressure on the gland caused pus to exude from the opening of the duct. Culture of this pus showed *Staphylococcus aureus hemolyticus*. Blood examination gave hemoglobin, 75 per cent; red blood cells, 3,800,000; white blood cells, 18,000 with 64 per cent neutrophiles. The treatment was dry heat to the face and pressure on the gland at frequent intervals to evacuate the pus.

On the tenth day of life the child's condition was grave. The swelling and edema covered the entire right side of the face, and he regurgitated all food and water. Sulfanilamide, 1 Gm. in twenty-four hours, was given. This caused considerable cyanosis which cleared on giving methylene blue. Within twenty-four hours the swelling began to subside and no more pus could be exuded on pressure. The blood

From the Department of Pediatrics, the University of Illinois (Rush), and the Presbyterian Hospital, and Women's and Children's Hospital, Chicago.

now showed hemoglobin, 75 per cent; red blood cells, 4,000,000; and white blood cells, 14,000. Improvement continued until the third week of life when a small indurated gland was noticed in the left cervical region. Four days later the right parotid gland again began to swell. Sulfanilamide was again given for three days, and the gland reduced in size. However, the cervical gland continued to enlarge and was incised two weeks after the beginning of the swelling. Cultures of the pus revealed the same type of organism found in the parotid gland. Following this, all the lesions healed well and the child was discharged at 6 weeks of age. He was treated in our syphilitic clinic for a year, and showed no ill effects from the parotitis.

CASE 2.—A white male infant was born normally of a primiparous mother, whose Wassermann and Kahn tests were negative. His weight was 5 pounds, 12 ounces. He was nursed every four hours and feedings were complemented by bottle. The progress was normal until the seventh day of life when the temperature rose to 101° F. and the infant nursed poorly. The following day (eighth day of life) the temperature was 102° F. and there was a definite enlargement of the parotid area on the right side. The blood showed hemoglobin, 90 per cent; red blood cells, 5,100,000; and white blood cells, 29,900. Sulfathiazole was given by mouth, 1 Gm. in twenty-four hours. The area enlarged and reddened and on the eleventh day of life was incised and one ounce of thick pus discharged. This contained *Staphylococcus aureus hemolyticus*. The discharge continued for two days when the sulfathiazole was stopped. The blood showed hemoglobin, 75 per cent, red blood cells, 4,700,000; white blood cells, 37,900. Twenty-four hours later, on the fourteenth day of life, the gland became enlarged again and was reopened and drained. The sulfathiazole was given again for two days, when the wound healed. The blood showed hemoglobin, 75 per cent, red blood cells, 4,500,000; and white blood cells, 17,800. Recovery was uneventful and the baby was discharged at three weeks of age, weighing 6 pounds, 5 ounces.

CASE 3.—A white male infant was born by cesarean section to a primiparous mother, whose Wassermann and Kahn tests were negative. The birth weight was 5 pounds, 8 ounces. The baby was given premature care and fed by gavage of lactic acid/breast milk. The child progressed normally until 8 days of age when the temperature rose to 101° F., and a swelling developed over the right parotid area. The blood showed hemoglobin, 75 per cent; red blood cells, 4,500,000; and white blood cells 30,000. One Gm. of sulfathiazole was given daily for four days. The gland was incised on the eleventh day of life and 25 c.c. of pus was obtained that cultured *Staphylococcus aureus hemolyticus*. The blood showed hemoglobin, 80 per cent, red blood cells, 4,800,000; and white blood cells, 26,500. The wound healed satisfactorily, but the child did not gain well for several weeks. At 1 month of age the blood showed hemoglobin 85 per cent; red blood cells, 4,600,000; and white blood cells, 28,300. The child was discharged at 6 weeks of age, weighing 6 pounds, 1 ounce. The blood now showed hemoglobin, 75 per cent; red blood cells, 3,600,000 and white blood cells, 14,300.

CASE 4.—A white male infant was born by low forceps to a primiparous mother, whose Wassermann and Kahn tests were negative.

The birth weight was 5 pounds, 13 ounces. His condition was good and he was given breast feedings complemented with a formula by bottle. There was some regurgitation at 4 days of age and 1/5000 of atropine was given by mouth before feeding for three days when the vomiting ceased. The child was circumcised on the eighth day of life. That evening the temperature was 101° F. and the next morning, the ninth day of life, it was 103° F. At this time a swelling was observed over the left parotid area. The blood showed hemoglobin, 100 per cent; red blood cells, 3,860,000; and white blood cells, 29,500 with 64 per cent neutrophiles. One Gm. of sulfadiazine was given by mouth in twenty-four hours for two days, the swelling increased and the temperature rose to 103° F. The medication was changed to sulfathiazole in the same quantity and the temperature fell to normal with swelling becoming fluctuant. The blood now showed 41,600 white cells. The gland was incised on the eleventh day of life and about 30 c.c. of purulent material was obtained which showed *Staphylococcus aureus hemolyticus* by culture. The gland slowly subsided in swelling and the child was discharged on the twenty-first day of life, weighing 6 pounds, 4 ounces. The white blood cells had fallen to 18,000.

CASE 5.—A white female infant was born normally to a multiparous mother, whose Wassermann and Kahn tests were negative. The birth weight was 8 pounds, 8 ounces. The child was given breast feedings and was never given a complement. At 7 days of age she was obtaining eighteen ounces of breast milk in twenty-four hours. On the eighth day of life the temperature rose to 103.6° F., and a swelling was noted over the left parotid area. The blood showed hemoglobin 90 per cent; red blood cells, 4,800,000; and white blood cells, 25,000 with 72 per cent neutrophiles. One Gm. of sulfathiazole was given in twenty-four hours for two days; by this time the swelling was fluctuating and was incised. The pus showed *Staphylococcus aureus hemolyticus*. An iodoform gauze was inserted which was removed in forty-eight hours. The blood showed hemoglobin, 80 per cent, red blood cells, 4,500,000 and white blood cells, 22,000. The discharge continued until the eighteenth day of life when the blood showed hemoglobin, 80 per cent, red blood cells, 4,500,000, and white blood cells, 12,400. During this time the mother's breasts had been pumped and the infant fed breast milk by bottle. She was discharged on the twentieth day of life, weighting 9 pounds, 8 ounces, and completely breast fed.

ETIOLOGY

The five infants described were born during a period of five years, in two hospitals delivering approximately 10,000 infants during that period. This gives our incidence as 1 in 2,000 infants. Bloch and Pacella stated that their two instances of purulent parotitis in the newborn occurred in 19,900 infants over a ten-year period. In going back over the records of both hospitals, we were unable to find any mention of purulent parotitis in newborn infants occurring before in a ten-year period; so our frequency stated may be too high. As to just why we should have had such an increase in these cases, we do not know. Certainly the nursery technique is considerably better at this time as judged by present-day standards than the former ten-year

period. There were no instances of any infection of any type on the maternity floor at the time these babies were stricken.

In our five cases in every instance the organism cultured was *Staphylococcus aureus hemolyticus*, which according to Torrey and Reese[5] is the predominating organism in the nasopharynx in 1- to 3-week-old infants and is a potential pathogen. The staphylococcus has been the most frequent organism reported although streptococcus, *Bacillus coli*, *Bacillus alcoligenes*, diplococci, and *Oidium albicans* have been found in the older reported cases. There are two explanations for the infection; one is by direct infection from the mouth, and the other is hematogenous. Probably both may occur, although the infection from the mouth seems more logical. However, why does this occur in certain instances and not in others? Baxter and MacDonald believed that in their infant, resuscitated with difficulty, wiping out the mouth with gauze was the cause. Three of our infants were delivered normally, one, by cesarean section, and one, by low forceps. None of these required resuscitation, and no gauze or catheters were used. Two of our infants were fed by tube, but we have fed premature infants in this manner for twenty years without such an incidence occurring. Two of the infants were fed by breast and bottle, and one never received anything except breast feeding.

Prematurity has been stated as a contributory cause. In going over the reported cases it was found that 65 per cent of the weights of the infants were more than, or the usual, weight of the newborn. In our series two of the infants were premature, two were small babies, and one weighed more than the usual newborn. This corresponds to the other reported cases of 35 to 40 per cent being in premature infants. Other contributory causes offered are poor condition and other infections. It is true that one of our infants was suffering from syphilis that might have lowered his resistance, but certainly the other infants were in good condition.

SYMPTOMS AND COURSE

The course and symptoms seem to be typical in all instances. There is first an unexplained rise in temperature from 101 to 104° F. This occurs from the fourth to the twelfth day of life in all reported instances, commonly at about 1 week of age. In every one of our infants it was first noted on the seventh or eighth day of life. Within twenty-four hours a swelling of the parotid is noted accompanied by heat and redness. There is also anorexia and some loss of weight. The blood shows a marked leucocytosis (18,000 to 40,000) which may increase for a few days. The leucocytes will average from 65 to 80 per cent of the total white cells. There is little, if any, change in the hemoglobin or red cells.

The course will now depend on the treatment. In the treatment outlined, the gland rapidly increases in size and becomes fluctuant in three or four days. It then heals rapidly after incision, and recovery occurs in one to two weeks. In about 35 to 50 per cent of the reported cases other glands became infected over the course of from two to three weeks. These were the opposite parotid and various cervical glands; in all of these the primary organism is usually found. This occurred in only one of our infants, the first. This child might be considered almost an untreated case, in which the symptomatic treatment corresponded to what was done to these cases formerly. In the same category is the discharge of pus through the duct into the mouth. This also happened only to our first case, which was probably the reason for the child's recovery. This is described in almost all of the reported cases where there was recovery.

TREATMENT

Formerly hot boric acid dressings were applied to the gland, and an attempt was made to express the pus from the duct. We did none of these in our last four cases. As soon as the diagnosis was made by the presence of the swelling over the parotid, sulfathiazole was given by mouth, 2 grains per pound in twenty-four hours in four doses. This was tolerated well and there were no reactions of any kind. We emphasize that sulfathiazole is the sulfonamide of choice. In one of our infants sulfadiazine was given for two days in error, and the infection spread rapidly. It began to localize as soon as the change to sulfathiazole was made. As soon as fluctuation is observed in the gland, a small incision is made at the lower border, just over the angle of the mandible. A probe is inserted and all pus pockets evacuated. An iodoform gauze drain is inserted simply to keep the wound open for forty-eight hours. Also to keep the wound open, a moist warm dressing is placed over the area. This is simply kept moist and not changed until the wound is examined. It may be necessary to open pus pockets later that have been missed the first time. In all of the older reported cases it is emphasized that incision of the gland may lead to salivary fistula. This has not occurred in any of our cases. Healing is prompt, leaving a small scar that is imperceptible after a few months. Three of these children have been followed for several years, and have had no difficulty of any kind.

The sulfathiazole should be continued as long as there is any drainage, or until the leucocyte count has fallen markedly. It was continued twelve days in Case 5. Inasmuch as daily blood examinations should be done, as well as urine examination, there should be no danger from an excess therapy.

In all of the older literature, the prognosis is given as bad, particularly for smaller babies. The mortality is stated as 50 per cent

in the average case. There was no mortality in our series, and our chief purpose in reporting these cases is to show that by treatment with sulfathiazole and incision at the proper time, that there is no reason that there should be.

It is also important that the general nutrition of the child should be maintained. Breast milk or its dilution with some well-digested food is essential. Our premature babies who were tube-fed were continued so. The larger babies are able to take a bottle if it is given slowly and carefully, or a dropper feeding can be used. Case 5 was completely breast fed. The infant was removed from breast and given her mother's milk pumped, by bottle On recovery she was replaced to the breast and left the hospital completely breast fed.

CONCLUSIONS

Five infants with purulent parotitis during the newborn period are added to those already reported, making a total of sixty-two cases. However, it is believed that this condition is much more frequent than its reported instance would indicate. A definite routine of treatment by administration of sulfathiazole and incision of the gland when fluctuation occurred, resulted in the recovery of all five cases.

REFERENCES

1. Plewka, W.: Arch. f. Kinderh., **69**: 279, 1921.
2. Elterich, T. O.: J. PEDIAT., **3**: 761, 1933.
3. Baxter, R. H., and MacDonald, M. T.: New England J. Med. **217**: 351, 1937.
4. Bloch, H., and Pacella, B. L.: Arch. Pediat. **54**: 68, 1937.
5. Torrey, John C., and Reese, M. K.: Am. J. Dis. Child **2**: 67, 1944.

952 NORTH MICHIGAN AVENUE.

DIAGNOSTIC METHODS IN WHOOPING COUGH

NELLES SILVERTHORNE, M.B., VIVIAN ZACKS, AND EFFIE JENKINS
TORONTO, ONTARIO

MANY studies in the past have demonstrated the value of the cough plate in the early diagnosis of whooping cough. Recently, Bradford and Slavin,[1] Brooks, Bradford and Berry,[2] and Miller and associates[3] demonstrated that nasopharyngeal cultures were superior to cough plate cultures in the diagnosis of whooping cough, particularly in infants. Cruickshank[4] found that the nasopharyngeal swab gave as good results as the cough plate in the bacteriologic diagnosis of pertussis. During the past two years we have had an opportunity of examining eighty-seven children for the presence of gram-negative bacilli by means of direct smear of nasal mucus, culture of nasal mucus, and cough plate cultures. The following report embodies the method and results of our studies.

METHODS AND MATERIALS USED

The children were not the best subjects on whom to test the efficacy of early diagnostic methods. They were, however, the only ones available for this study at the time. They were mainly a group of patients admitted to the Hospital for Sick Children usually with whooping cough or suspected whooping cough with the additional complication of bronchopneumonia. A few were those with suspected early cases who were tested at the laboratory. This fact explains why our cough plate percentage was not as high as previously reported.[5] In that publication we were able to examine a larger percentage of children in the first and second week of the disease.

Smears and cultures of nasal mucus were taken by means of a sterile rubber catheter inserted into the patient's nostril similar to the method of Auger.[6] A 20 c.c. syringe was attached to the end of the rubber catheter and suction applied to obtain nasal mucus. After nasal mucus was obtained in this manner the rubber tubing was returned to a sterile test tube (Fig. 1). A culture of the nasal mucus was then made on Bordet medium and the material spread with a glass spreader and incubated two to four days. From the nasal mucus thus procured, direct smears were made on glass slides and examined microscopically after staining by Gram's method. The cough plates were taken in triplicate in the usual manner and incubated two to five days. The smears of nasal mucus were examined immediately for the presence of gram-negative bacilli. The cultures of nasal mucus and cough plate cultures were examined at two-, three-, four- and five-day intervals after incubation. Any suspicious colonies were picked and examined micro-

From the Wards and Laboratories of the Hospital for Sick Children, the Department of Paeditrics, University of Toronto, under the direction of Alan Brown, M.D., F.R.C.P. (London), and the Connaught Laboratories, University of Toronto.

TABLE I

RESULTS OF EXAMINATION OF CHILDREN FOR PRESENCE OF H. PERTUSSIS

NUMBER EXAMINED	CLINICAL	DIRECT SMEAR OF NASAL MUCUS	CULTURE OF NASAL MUCUS	COUGH PLATE CULTURE
33	Not pertussis	29 negative 4 showed gram-negative bacilli	All negative	All negative
54	Pertussis	44 showed gram-negative bacilli 8 negative 2 questionable	23 positive 31 negative	30 positive 24 negative

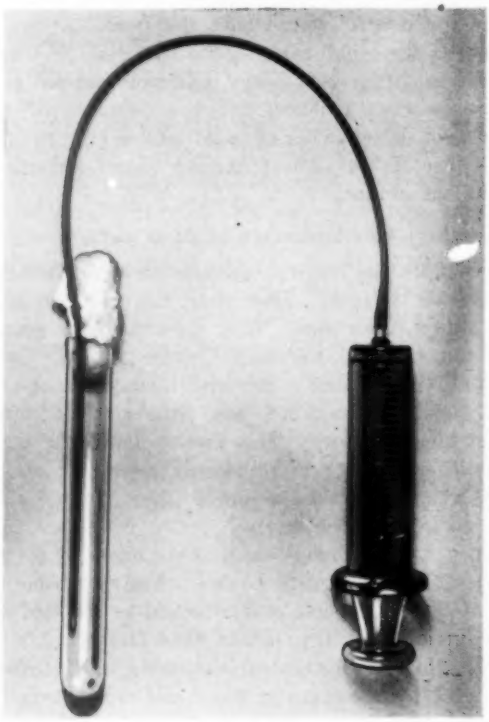

FIG. 1.

scopically to see if they were *Hemophilus pertussis.* Agglutination with phase I rabbit serum was carried out to confirm that the culture was one of *Hemophilus pertussis.* In some instances the culture of nasal mucus showed a predominant growth of *Hemophilus pertussis* (Fig. 2). The results of our investigations are shown in Table I.

DISCUSSION

From Table I the following results are noteworthy: Of the thirty-three children examined who did not have clinical whooping cough,

four showed the presence of gram-negative bacilli in the film of nasal mucus; all cultures of nasal mucus and cough plates were negative for *Hemophilus pertussis*. Of the fifty-four children examined who had clinical whooping cough, forty-four showed the presence of gram-negative bacilli in a direct film of nasal mucus, eight films were negative and two films were questionable. Of the fifty-four cases of whooping cough, twenty-three cultures of nasal mucus were positive and thirty-one were negative. Of the fifty-four cases of whooping cough thirty cough plate cultures were positive and twenty-four were negative. In other

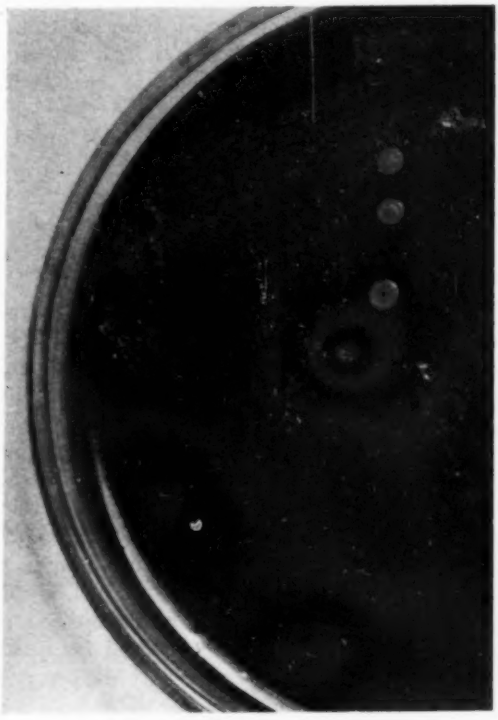

Fig. 2.

words, from the total series of fifty-four cases of whooping cough, cough plate cultures (taken in triplicate) were positive in 55 per cent of instances, whereas cultures of nasal mucus were positive in 42 per cent of instances. These results are those concerned with all ages (from 7 weeks to 14 years) of the children examined. Of the thirty-five patients with clinical whooping cough, 2 years of age and under, thirty-three revealed gram-negative bacilli in the direct films of nasal mucus, seventeen cultures of nasal mucus were positive for *Hemophilus pertussis* and twenty-two cough plate cultures were positive. In other words, of

the thirty-five patients 2 years of age and under with clinical whooping cough, 62 per cent of cough plate cultures (taken in triplicate) were positive as compared to 48 per cent of cultures of nasal mucus. From this small series it would appear that the cough plate culture method (cough plates taken in triplicate) is superior in isolating *Hemophilus pertussis* to the method we employed in securing cultures of nasal mucus. This finding applies to older children as well as to those 2 years of age and under. We have found that both methods were superior to either one alone, an observation made by Miller and associates.[3] An explanation for the discrepancy that exists between our results and those of earlier publications[1, 2, 3] may be obtained from the following facts. First, we used cough plates in triplicate and have been using them quite consistently over ten years. Second, the method by which we obtained nasal mucus was different from that of other authors. However, we do believe this method of obtaining nasal mucus may be of value, if it is desirable to transport cultures from place to place, as an adequate amount of nasal mucus is obtained to allow for nasal smear and culture. Another finding of possible significance is that of the thirty-three children examined who did not have clinical whooping cough, twenty-nine films of the nasal mucus were negative for gram-negative bacilli whereas in fifty-four clinical cases of whooping cough, forty-four showed the presence of gram-negative bacilli in films of nasal mucus. In ten instances of clinical whooping cough large numbers of gram-negative bacilli were seen in the direct films of nasal mucus with practically no other microscopic forms. We believe these findings are significant enough to suggest that an examination of the film of nasal mucus may give one a preliminary indication that the case is one of whooping cough. However, it is not accurate enough without a confirmatory culture, since *Hemophilus influenzae* is also found in culture when gram-negative bacilli are seen in smears. Although the results with nasal mucus cultures are not as efficient in our hands as cough plate cultures in isolating *Hemophilus pertussis*, we believe that it is much simpler to obtain material for nasal mucus cultures than for cough plate cultures especially in young infants. In Fig. 2 a culture of the nasal mucus from a child reveals a predominant growth of *Hemophilus pertussis*. Most cultures of nasal mucus do not give one as profuse a growth as is seen in this photograph. One infant with a history of whooping cough for one week's duration revealed many gram-negative bacilli in the direct film of nasal mucus with practically no other bacterial forms. The cultures of both nasal mucus and the cough plates from this infant were very obviously positive. Recently we have had patients in the first two weeks of the disease before any complicating pneumonia was present in whom the film of nasal mucus has revealed predominant numbers of gram-negative bacilli. It would appear that the results from direct smear will be helpful in early diagnosis if the case is obtained early.

SUMMARY

1. Direct smear of nasal mucus has revealed gram-negative bacilli in 80 per cent of patients with known whooping cough as compared to 12 per cent in cases not suffering from whooping cough.

2. Cough plate cultures (taken in triplicate) were positive for *Hemophilus pertussis* in 55 per cent of instances compared to cultures of nasal mucus which were positive in 42 per cent of the cases.

3. Both culture methods used simultaneously were found to be superior in isolating *Hemophilus pertussis* to either one alone.

In conclusion, it is felt that direct smears of nasal mucus in the early stage of whooping cough are helpful but not infallible in obtaining preliminary evidence in the diagnosis of the disease. With our technique cough plate cultures (taken in triplicate) are superior to nasal mucus cultures in isolating *Hemophilus pertussis* from patients with whooping cough at any age up to 14 years.

REFERENCES

1. Bradford, William L., and Slavin, Betty: Proc. Soc. Exper. Biol. & Med. 43: 590, 1940.
2. Brooks, Anne M., Bradford, William L., and Berry, George P.: J. A. M. A. 120: 883, 1942.
3. Miller, John J., Leach, Charles W., Saito, T. M., and Humber, J. B.: Am. J. Pub. Health 33: July, 1943.
4. Cruickshank, Robert: Lancet 246: 176, 1944.
5. Silverthorne, Nelles, Fraser, Donald T., and Hendren, Gordon: Canad. M. A. J. 38: 556, 1938.
6. Auger, W. J.: J. PEDIAT. 15: 640, 1939.

ELECTROCARDIOGRAPHIC STUDIES IN ASTHMATIC CHILDREN

H. T. Engelhardt, M.D., and V. J. Derbes, M.D.
New Orleans, La.

IN A previous communication we[1] have presented evidence which tended to show that uncomplicated bronchial asthma is not a factor in the production of heart disease. Our material was essentially the same as that formerly used[1] and consisted of seventeen children with an average age of 9.3 years; the youngest being five and the oldest 14 years old. The average duration of the asthma was 4.7 years, with a minimum duration of 14 months and a maximum of 9 years. The first study concerned itself with an evaluation of roentgenologic data. Standard methods of estimating heart size from x-ray examination were used. After preliminary fluoroscopy, two meter plates employing standard technique, were taken on all subjects. The usual measurements of the cardiac silhouette were obtained. In addition, prediction formulas using height and weight for the transverse diameter of the heart were struck. Further, data relating to the cardiothoracic ratio of Danzer[2] were obtained. The cardiac area was estimated by applying the data to the Eyster-Hodges[3] nomogram of cardiac area for children. These children after having been subjected to a complete allergic diagnostic survey were then subjected to a careful physical examination with particular reference to manifestations of cardiac and pulmonary disease.

Although the literature on roentgen examination of the heart in asthmatic children is extremely scant there is even less information on the electrocardiographic manifestations of such children. We, therefore, made tracings employing the conventional three leads as these data could be compared with previous studies.[4, 5, 6, 7, 8] In addition, the precordial leads CF_1, CF_2, CF_3, CF_4, and CF_5 were taken on each subject exercising the criteria prescribed by the American Heart Association and the Cardiac Society of Great Britain and Ireland.[8, 9] In contrast to the standard leads, no comparable information concerning the chest leads of normal children was available.

FINDINGS IN STANDARD LEADS

The Heart Rate.—The heart rate ranged from 70 to 110 beats per minute, the mean for the group being 89. Hafkesbring and associates[4] pointed out that a certain variation at each age is to be expected, but the fluctuation in rate has no important bearing on the electrocardiographic findings.

The P Wave.—In the standard leads the amplitude and duration were determined. The average amplitude of the P wave in Lead I was

From the Department of Medicine, Tulane Medical School.

0.89 mm.; in Lead II, 1.35 mm.; in Lead III, 0.44 mm. The duration of the P wave in Lead I was 0.075 second; in Lead II, 0.08; in Lead III, 0.065.

Comparison of the heights of P waves in our asthmatic children with those of normal children of Hafkesbring and associates is set forth in Table I.

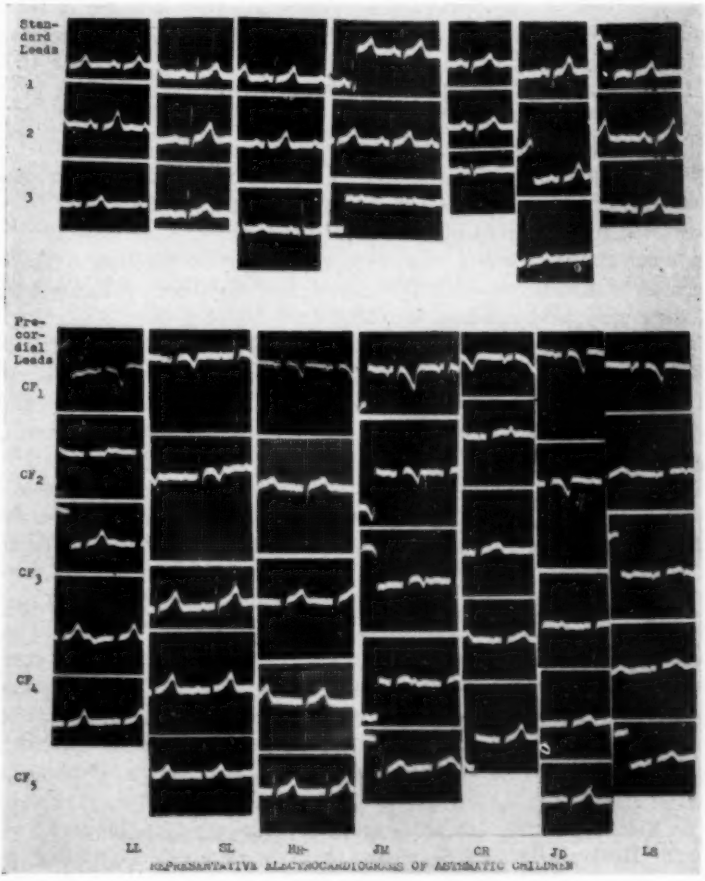

Fig. 1.

The P-R Interval.—Our average P-R interval for Lead I was 0.144 second; for Lead II, 0.113; and for Lead III, 0.16 second. These findings compare well with those of Krumbhaar and Jenks,[5] who found in their normal children that the P-R interval varied from 0.12 to 0.16 second. Seham[6] stated that the upper limit of normal for older children was 0.18 second, while Hafkesbring and associates found 0.165 second to be the upper limit for their older children.

TABLE I

	ASTHMATIC CHILDREN	NORMAL CHILDREN
P_1	0.89	0.70
P_2	1.35	1.31
P_3	0.44	0.58

The direction of the P wave was upright in every instance in Leads I and II; in Lead III all were upright except six which were diphasic, of the plus-minus type. These figures compare very closely with those of Hafkesbring and associates who found upright P waves in every case in Leads I and II and 4 per cent inverted and 2 per cent diphasic of the plus-minus type in Lead III. There is considerable variation in the literature as to the direction of P_3, Lincoln and Nicolson[7] finding in 3.2 per cent of their cases an inversion of P_3 while Perry[8] found P_3 inverted in 8 per cent of his cases.

In none of the P waves was there any abnormal notching. This is in complete agreement with the experience of others. (Hafkesbring and associates,[4] and Ashman and Hull[10]).

The QRS Complex.—We found that the QRS complex in Lead I was 0.075 second; in Lead II, 0.079; and in Lead III, 0.081. Hafkesbring and associates reported their average value to be 0.065. Our values more nearly approach those of McGinn and White[11] who reported an average of 0.071.

The Q Wave.—The Q wave in Lead I was found to be 0.29 mm.; in Lead II, 0.50 mm.; in Lead III, 0.68 mm. This is general agreement with other workers who found the Q wave depth increased from Lead I to Lead III.

The R Wave.—We found the average height of the R wave in Lead I to be 6.2 mm.; in Lead II, 11.8 mm.; and in Lead III, 7.0 mm. These values for R waves are lower than those found by Seham,[6] but correspond closely with those of other observers.[4]

The S Wave.—The averages for the S wave in each lead are as follows: S_1, 1.6 mm.; S_2, 1.85 mm.; and S_3, 1.0 mm. In none of these components of the QRS complex was there any degree of abnormal slurring.

The Electrical Axis.—In order that our data might be compared with those of Hafkesbring and associates the axes were calculated from the chart constructed by Dieuaide.[12] The arithmetical mean was 64°. This compares with the findings of workers previously quoted.

The S-T Interval.—This segment in Lead I measured 0.28 second; in Lead II it measured 0.25 second; in Lead III, 0.26 second. There was no significant shift of the S-T segment, all shifts being under 1 mm.

The T Wave.—Table II presents a comparison of our data with those of Hafkesbring and associates for the height of the T waves. T_3 was found to be isoelectric in 20 per cent of our cases and inverted in 5.8 per cent. Perry[8] found T_3 to be negative in 54 per cent while Seham found T_3 inverted in 15 per cent of normal children.

TABLE II

	ASTHMATIC CHILDREN	NORMAL CHILDREN
T_1	2.67 mm.	2.18 mm.
T_2	3.5 mm.	2.41 mm.
T_3	0.94 mm.	0.16 mm.

FINDINGS IN PRECORDIAL LEADS

Lead CF_1.—The amplitude of the P wave varied from –2.0 mm. to +0.5 mm. with an arithmetical mean of –0.32 mm. There were no Q waves. The R wave measured from 2 to 12 mm., with an arithmetical mean of +6 mm. The S wave measured from 6 to 25 mm. with an average of +16.7 mm. The T waves ranged from –6 to +4 mm. with an arithmetical mean of –3.29 mm.

Lead CF_2.—The amplitude of the P wave varied from –1.75 mm. to +0.5 with an arithmetical mean of +0.43 mm. There were no Q waves. The R wave measured from 6 to 15 mm. with an average of +10 mm., thus tending to be higher than the R wave of CF_1. The S wave varied from 6 to 32 mm. with an average of +20.2. The T wave ranged from –6 to +5 mm. with an average of –1.32 mm. indicating a more positive direction for this component.

Lead CF_3.—The amplitude of the P wave varied from –1.0 mm. to +0.5 with an arithmetical mean of 0.33 mm. The Q wave was again absent. The R wave measured from 6 to 11 mm. with an average of +8.8 mm. The S wave measured from 4 to 17 mm. with an average of +13.1 mm. The T wave ranged from –4.0 to +5.0 mm. with an arithmetical mean of 1.19 mm.

Lead CF_4.—The amplitude of the P wave varied from –1.0 to +0.25 mm. with an average of –0.15 mm. The Q wave varied between 0 and 1 mm. with an average of +0.11. The R wave measured from 5 to 20 mm. with an average of +10.8 mm. The S wave varied from 4.5 to 17 mm. with an average of +9.90. The T wave ranged from –3.5 mm. to +5.0 with an arithmetical mean of +2.09.

Lead CF_5.—The amplitude of the P wave varied from –1.0 to +2.0 mm. with an average of +0.10. The Q wave ranged from 0 to 2 mm. with an average of +0.27. The R wave measured from 4 to 12 mm. with an average of +7.08. The S wave varied from 2 to 15 mm. with an average of +4.85. The T wave ranged from +1.0 to 5.0 with an average of +2.67 mm.

SUMMARY AND CONCLUSIONS

The standard leads in the asthmatic children studied are in agreement with the control data of other workers[13] who studied normal children. The precordial leads compare well with those of normal adults found by others although the R wave in CF_5 measured less than the R wave in CF_2, CF_3, and CF_4. The average height of the R wave in CF_5 was, however, within the limits delineated by others who have

studied adults.[13] As expected, sinus arrhythmia was encountered frequently. There were no abnormal variations in rhythm in any of the patients studied.

These data confirm those found in our previous study. They tend to indicate that in children uncomplicated bronchial asthma with an average duration of 4.7 years is not a factor in the production of heart diseases.

REFERENCES

1. Derbes, V. J., and Engelhardt, H. T.: Roentgen Studies of the Heart in Asthmatic Children, J. PEDIAT. **25**: 394, 1944.
2. Danzer, C. S.: Am. J. M. Sc. **157**: 520, 1919.
3. Hodges, P. C., Adams, W., and Gordon, W.: J. A. M. A. **101**: 914, 1933.
4. Hafkesbring, E. M., Drawe, C. E., and Ashman, R.: Am. J. Dis. Child. **53**: 1457, 1937.
5. Krumbhaar, E. B., and Jenks, H. H.: Heart **6**: 189, 1917.
6. Seham, M.: Am. J. Dis. Child. **21**: 247, 1921.
7. Lincoln, E. M., and Nicolson, S. H. B.: Am. J. Dis. Child. **35**: 1001, 1928.
8. Perry, C. B.: Arch. Dis. Childhood **6**: 259, 1931.
9. Joint Recommendations of the American Heart Association and the Cardiac Society of Great Britain and Ireland, Am. Heart J. **15**: 493, 1938.
10. Ashman, R., and Hull, E.: Essentials of Electrocardiography, ed. 2, New York, 1941, The Macmillan Co., p. 78.
11. McGinn, S., and White, P. D.: Am. Heart J. **9**: 642, 1934.
12. Dieuaide, F. R.: Arch. Int. Med. **27**: 588, 1921.
13. Schanno, R. L.: Am. Heart J. **19**: 713, 1940.

WHAT IS THE GUILLAIN-BARRÉ SYNDROME?

A Study of the Underlying Pathological Lesions

Frederic H. Lewey, M.D.
Philadelphia, Pa.

A FASHION has recently developed in this country of designating all kinds of polyneuritides, polyneuropathies, and ascending paralyses of radicular or spinal nature as Guillain-Barré syndrome. This tendency to unite a heterogeneous clinical and pathological material under a noncommittal title has led to a result exactly opposite to the original intention of Guillain, Barré, and Strohl[1] in describing the specific type of radiculoneuritis which bears their names today.

A small epidemic of polyneuritis and radiculitis was observed during the years 1916 to 1918 among the Allied Armies in France and described by French, English, and American neurologists. Guillain, Barré, and Strohl[1] were the *first* to publish their observations based on only two patients. They stressed three distinct peculiarities observed in their patients: (1) An albuminocytologic dissociation, that is, a high protein content of the spinal fluid without marked increase of cells; (2) preponderance of motor weakness over the signs, mostly subjective, of sensory disturbances; (3) a remarkably rapid and complete recovery of the patients despite their initial serious appearance.

In contrast to these widely confirmed findings, Bradford, Bashford, and Wilson[2] described a *second group* of patients consisting of thirty cases of acute infectious polyneuritis, which showed a mortality of 26.6 per cent and a spinal fluid "free from cells and without abnormalities," at least in the four patients in which it was examined.

The *third group* of cases of this epidemic which forms the basis of Holmes' and Kennedy's publications has been designated by Casamajor[3] as acute ascending paralysis, that is, as part of the Landry syndrome. These patients showed a normal spinal fluid, and the course of their disease was by no means so benign as Guillain had postulated.

A *fourth group* of patients was likened to the Guillain-Barré syndrome by Taylor and McDonald[4] who in fifteen of sixteen persons with polyneuritis observed facial diplegia. Patrick had previously pointed to this combination without connection with the Guillain-Barré syndrome. The spinal fluid findings varied in this group from normal to a typical dissociation, and death from respiratory complication occurred occasionally.

Numerous cases of polyneuritis in children and adults have been linked up with the Guillain-Barré syndrome (Gillespie and Field,[5] Hy-

From the Pediatric and Neurosurgical Services and the Neuropathological Laboratory of the Hospital of the University of Pennsylvania.

Read by invitation at the Joint Meeting of the Pediatric and Pathological Societies of Philadelphia on Jan. 13, 1943.

land and Russel,[6] Gaertner,[7] Strauss and Rabiner[8]) during the period between World War I and II. In some of them the spinal fluid was either not examined at all or not adequately,[8a] or it was found normal.[8b] Other patients died or belonged obviously to the Landry group.

Guillain,[9] in reviewing the situation in November, 1936, refused emphatically to accept any of these four groups as members of his syndrome. He restated his previous criteria on the basis of numerous new observations and added further specifications. He declined that he or any of his co-workers had seen unilateral or bilateral facial paralysis accompanying his syndrome and insisted that he had not heard of a single death among the patients of his group. Finally, he postulated a protein content of from 1,000 to 2,000 mg. per cent in the spinal fluid and declared cases with not more than from 300 to 400 mg. per cent as either abortive forms or not part of his syndrome.

If these protein values were generally accepted as conditio sine qua none of the diagnosis the majority of patients attributed to the Guillain-Barré syndrome (De Jong,[10] Gilpin, Moersch, and Kernohan[11] and Bassoe[12]) had to be eliminated. However, Cobb[11a] as well as Moersch did not consider it justifiable to limit the protein values of the spinal fluid so sharply--especially when only one examination had been performed—because of their changes in the course of the disease.

All such minor details became insignificant when Guillain,[13] in the following year (1937), as chairman of a symposium on radiculoneuritis in Brussels, was compelled to synthesize the result of the discussion and withdrew all his previous specifications.

The albuminocytological dissociation which in 1916 had indeed been an important discovery had in the meantime been recognized as one of the characteristics of a partial block caused by the arachnitis. Its presence did not speak in favor of a special form of polyneuropathy nor its absence against it when the tap was performed in the first days of the disease.

In addition to the classical clinical form, three more hitherto-banned disease pictures were admitted into the Guillain-Barré syndrome: namely, a mixed spinal and mesencephalic type, including the participation of all cranial motor nerves, unilateral and bilateral facial paralysis being especially frequent; a pure mesencephalic form; a form with later mental signs. All these variations had been observed in the meantime by Guillain personally and by many of his co-workers.

Guillain still stressed that he had never seen nor heard of a single instance of death in patients suffering from his syndrome, but admitted that, when out of luck, "one might even die of chicken pox." This capitulation seems not to have been sweeping enough for he continued that the above-mentioned epidemics with high mortality could not *yet* be included into his syndrome until more was known of their etiology.

Hence, nothing was left of the Guillain-Barré syndrome beyond what was known for scores of years; namely, that certain polyneuropathies might involve one or more cranial nerves and encroach upon the roots and even the central nervous system itself, and that this disease was sometimes benign and at other times malignant. The question of the albuminocytologic dissociation had shifted in that its presence suggested a virus infection without establishing it.

The last possibility of saving the disease entity of the Guillain-Barré syndrome consisted, in ignorance of the etiology of any of these various forms, in demonstrating its uniform pathologic basis. It may appear preposterous to speak of the histopathology of a disease which by definition does not end lethally. However, a critical survey of the meager literature seems to bear out just this point.

Necropsies of patients with conditions diagnosed as acute ascending paralyses (Casamajor[3]), polyneuroradiculitis ascendens (Gaertner), acute infectious neuritis (Bradford, Bashford, Wilson[2]), Landry's ascending paralysis or polyneuritis with facial diplegia (Taylor and McDonald[4]) showed true inflammatory signs: infiltration of the peripheral nerves and the arachnoid with lymphocytes and accumulation of them around the anterior horn cells, patchy demyelination of the nerve fibers and preservation of the axis cylinders.

One biopsy and four necropsies represent the total unequivocal histopathologic material found in the literature of cases included in the clinical picture of the Guillain-Barré syndrome. In the first instance, reported by Bassoe,[12] numerous tortuous veins were seen in operation overlying the spinal cord as the only abnormality. Complete recovery followed after seven years. Congestion of the blood vessels and numerous minute hemorrhages in the anterior and posterior roots were the only histopathologic findings in a man of 68 seen by Balduzzi[14] with a typical clinical picture; while Gilpin, Moersch, and Kernohan[11] found demyelination of the peripheral nerves and posterior roots and fragmentation of the axis cylinders in a patient of this group who died of respiratory complications. The central nervous system was normal. In the two cases of Roseman and Aring[15] the peripheral nerves were the primary site of damage in the nervous system. There were ganglionic and neuronal changes widespread in the central nervous system but they appeared rather mild and could be considered as irreversible. In fact, most of the changes in spinal cord and brain stem appeared to represent reactions to the injuries in the peripheral nerves rather than primary foci. Description and photomicrograms of the changes in the peripheral nerves in these cases suggest that these changes were similar to, if not identical with, our own findings, though much milder.

Our own histopathologic material was gained, first, in operation under conditions similar to those present in Bassoe's patient and, second, in necropsy. The latter was performed in a child who died unexpectedly of a rare complication after having seemingly recovered.

CASE 1.—H. Y. (51394, Hospital of the University of Pennsylvania) was admitted to the neurosurgical department July 4, 1942, with the following history: The 29-year-old man weighing 335 pounds, had been in his usual good health until three and one-half weeks previously when he had wakened in the morning with pain in his back, his left leg, and the left side of his buttocks. The pain was of burning quality and became worse when stretching the leg or the back. There was no weakness; bladder and bowels functioned normally. He consulted a doctor and several osteopaths to no avail. Following manipulation of his leg by a chiropractor pain subsided for a week. When it returned he saw a naturopath who applied electricity through the rectum. Following this treatment the left side of the penis and scrotum and the left leg became numb, and patient was unable to urinate or defecate. The numbness descended along the left leg to the foot and a severe burning pain appeared in the numb parts. Drugs produced an involuntary bowel movement and drippling of urine the day before admission. Since that time he had been unable to empty the bladder. He consulted Dr. J. J. Reilly in Camden who sent him to the hospital.

Neurologic examination showed absence of the left Achilles jerk and decrease of the left knee jerk. There was no weakness or pyramidal signs. All modalities of sensation were dulled and decreased but none absent in the left leg, left side of scrotum, penis, and buttocks. No definite segmentary distribution and no upper limit of the sensory disturbance could be delineated. There was no tenderness of nerve trunks.

Urine, 1,000 c.c., was removed by catheter and an indwelling catheter left. Cystoscopy failed to show an obstacle in the urethra or prostate. The bladder showed inflammation of the walls, the urine was infected with *Streptococcus mucosus capsulatus*. Cystometric measurement revealed a cord bladder.

The spinal fluid was clear, containing 140 mg. per cent protein and four cells.

X-ray examination after lipiodol injection showed a complete block half way between the fourth and fifth lumbar interspace.

The diagnosis which so far had been tentatively "Guillain-Barré syndrome" shifted now to obstructive process in the cauda equina.

Operation (July 15, 1942) showed no extradural mass to account for the defect in the lipiodol column. The dura was opened and no spinal fluid or lipiodol obtained. No tumor was present. The roots of the cauda equina were matted together and tightly bound up with the arachnoid. The roots were carefully freed from their adhesions and from one another, and with this maneuver spinal fluid and lipiodol gushed forward. Two roots which were specifically swollen and red were removed for biopsy.

The pain disappeared the day after the operation. The recovery was fairly stormy because of the infected bladder, requiring tidal

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Figs. 1 and 2, H. Y.; Figs. 3 and 4, B. J. F.—Sacral roots. Figs. 1 and 2 show an unusual degree of peracute, noninflammatory neuropathy. The myelin has completely broken down; it appears as an amorphous, powderlike substance though still in place. The axis cylinders are equally damaged, only a few are of normal size, the majority thin and poorly impregnated. The Schwann apparatus appears normal in some places, proliferated in others and destroyed in a last group. A dense mesodermal scar has practically replaced the parenchyma. Figs. 3 and 4 show a similar picture though a less fulminant process. The myelin sheaths are swollen and degenerated, the thick fibers being more involved than the thin ones. The axis cylinders are slightly less involved but many are unraveled, swollen and in some places fragmented. Some fibers show club formation. At the left side of the picture a bundle of very fine axis cylinders is visible, which, however, does not give indication of new formation. The Schwann cells are in proliferation. No mesodermal scar has been formed so far. Figs. 1 and 3, phosphotungstic acid; Figs. 2 and 4, Bodian. ×300.

Fig. 1.

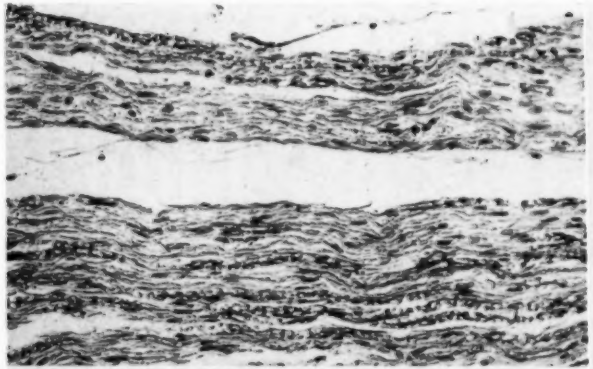
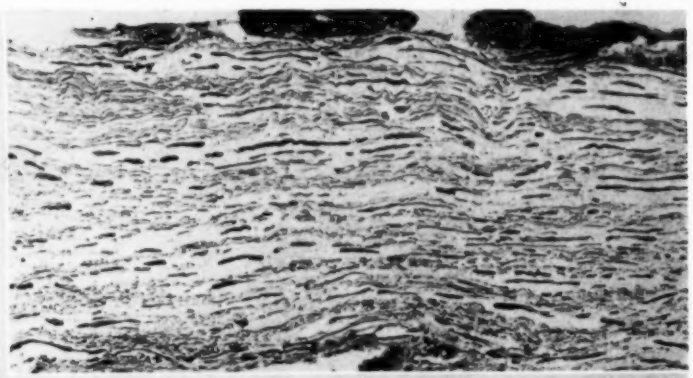


Fig. 2.



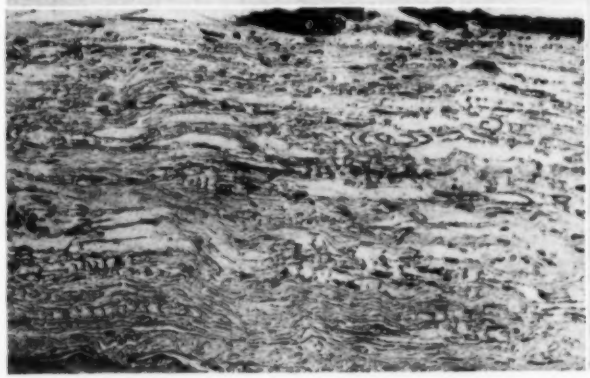


Fig. 3.

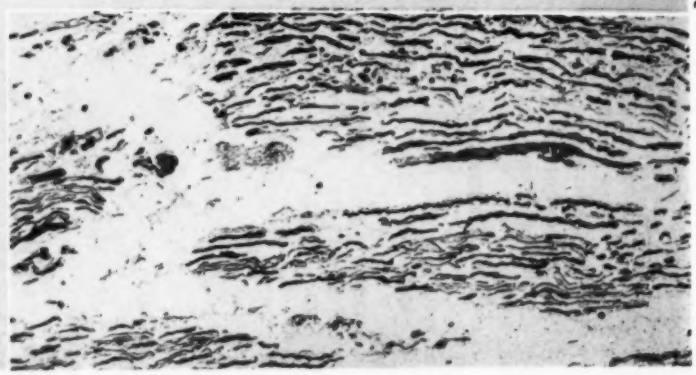


Fig. 4.

Figs. 1-4.—*(For legends see opposite page.)*

drainage, incontinence of stool, and the weight of the patient which retarded healing of the operative wound. Nevertheless, on the eighth postoperative day the patient passed urine and stool voluntarily for the first time since the onset of his illness, and experienced four days later his first erection in seven weeks.

He left the hospital four weeks after admission (Aug. 5, 1942) completely recovered except for a few open suture points at the line of his incision.

Histological examination of the two posterior roots removed in biopsy (Figs. 1 and 2) revealed an unusual degree of peracute, noninflammatory neuropathy. The myelin and the neurokeratin framework of almost all nerve fibers had broken down and disappeared. What was left of the myelin sheaths had a powder-like appearance. No compound granular bodies were found anywhere. The axis cylinders were unraveled, partially swollen, partially fragmented. The Schwann apparatus was unaffected in some fibers, proliferated in others, and destroyed in the rest. Endoneurium and perineurium had overgrown the whole root, indicating the degree of mesodermal scar formation.

Pathologic diagnosis was fulminant radiculopathy.

CASE 2.—B. J. F. (46569 and 41-48758 University of Pennsylvania Hospital), a well-nourished girl of 3½ years, was in good health until Dec. 20, 1940, when she developed a mild uncomplicated head cold. Three days later she began to complain of pain in her buttocks in the region of the exit of the sciatic nerves. The same afternoon she sat down heavily on the ice but was able to walk home and climb the stairs. On the two following days she complained of stiffness of the back and was unwilling to bend forward. She began to stumble and fall and could not keep balance. She was seen Dec. 26 and 27 by a pediatrician and an orthopedist who found hyperextension of the spine and resistance to bending forward, staggering gait, gross ataxia in the finger-to-nose test, absence of all tendon reflexes, but presence of the abdominal reflexes and no pyramidal signs. She was kept in bed for the following three days. When placed on her feet thereafter the legs buckled under her. She cried in her sleep and showed marked change of personality. Temperature was checked daily both when the patient was in the hospital and at home and was normal throughout the disease. She was suspected of a midline cerebellar tumor and was admitted to the neurosurgical ward December 30.

On admission she complained of pain in the eyes and buttocks and was unable to stand, while sitting was possible with difficulty. The tonsils were large but not infected. The physical examination was otherwise negative. On Jan. 3, 1941, she was free from pain, and cranial nerves were normal. There was weakness in the muscles of all extremities. The fingers were held partly flexed. Dorsiflexion of wrist and grip was very weak. There was slight contraction of the gastrocnemius muscles. Leg movements were made with fair power. All tendon reflexes in arms and legs were absent. Abdominal reflexes now also were absent. There were no pyramidal signs. She was willing at times to stand but was entirely unable to support herself, "the knees gave way." There was marked hypotonia. The spontaneous motility of the legs in recumbent position, the facility to turn from one side to the other, and her playfulness and attentiveness were in

strange contrast to the complete inability to righten herself and to stand. The sensibility for touch and prick appeared to be normal. Vibratory sense was normal on head, sternum, and elbows, but absent in hands and legs.

All laboratory examinations including those for lead and porphyrines were negative as were x-ray examination of head and spine. Spinal fluid showed on two taps 210 and 160 mg. per cent protein, respectively, with one and two cells.

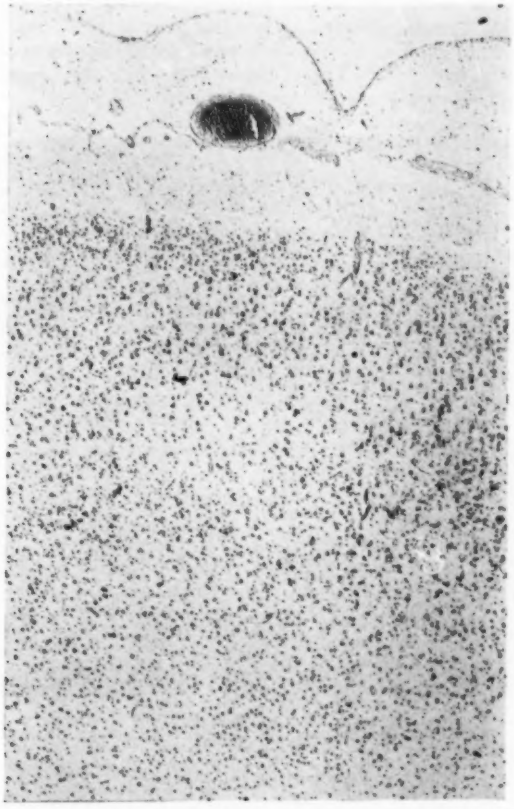


Fig. 5.—B. J. F. The arachnoid of the cortex is considerably thickened and shows scattered depots of hemosiderin. The underlying glia has formed a dense carpet extending into the external granular layer. The cortex shows some warping of its layers and a number of nerve cells in chronic disease. The blood vessels are moderately fibrotic. Cresyl violet. ×37.

In the absence of any indication of increased intracranial pressure it was decided that the girl was not suffering from a cerebellar tumor but from polyneuroradiculopathy, possibly encroaching slightly upon the cord, of the Guillain-Barré type. She was transferred to the children's ward where she was seen by Dr. Joseph Stokes, Jr. She was given thiamine chloride by injection beginning January 8; first 50 mg., later 100 mg. daily.

The patient improved remarkably until January 15. She seemed much brighter, the extremities much stronger and less tender. She seemed almost recovered. During her stay in the hospital the rectal temperature had varied between 98 and 99° F. On the afternoon of January 15, it rose suddenly to 100.2°, a faint maculo-erythematous rash appeared on the chest and around the mouth, the throat was red and inflamed. A culture was made but failed to grow hemolytic streptococci. At 9:30 of the same evening deep, prolonged, laboring respiration of the thoracic type was observed without participation of the diaphragm. The child was perfectly conscious and in no pain. Bronchoscopic examination revealed no obstruction or pulmonary collapse. Some purulent bronchial secretion contained *Micrococcus catarrhalis*. At about 10 P.M. the child stopped breathing while the heart continued under artificial respiration and oxygen until 10:30.

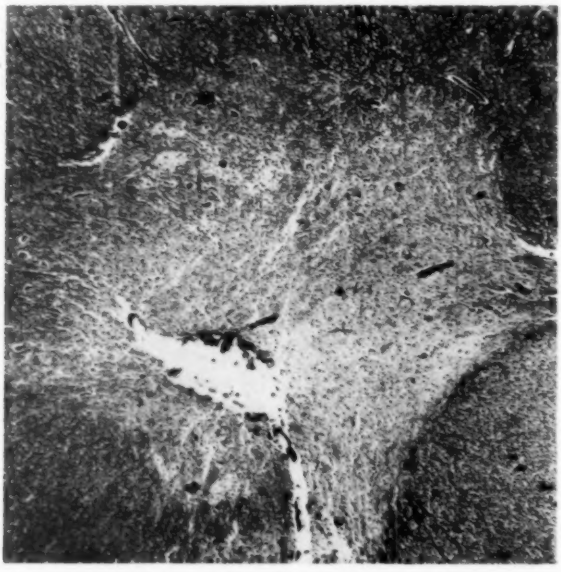


Fig. 6.—B. J. F. Anterior horn of cervical cord. Only a few nerve cells are preserved and the glia fibers are increased in number. Numerous small and one large cavity have formed around blood vessels with hemosiderin deposits and perivascular gliosis. This process has terminated and may have been of inflammatory or degenerative nature in the beginning. Phosphotungstic acid. ×37.

Necropsy showed hemorrhagic bronchitis and patchy pulmonary edema with collapse of the right lower lobe, hyperplasia of the mesenterial lymph nodes.

The arachnoid was considerably thickened over most gyri of both hemispheres. The underlying marginal glia of the cortex (Fig. 5) had in some places formed a dense carpet extending into the external

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Fig. 7, the right; Figs. 8 and 9, the left phrenic nerve, of B. J. F. The *right phrenic nerve* shows a marked loss of myelin fibers among a great number of fairly well-preserved myelinated axis cylinders. The *left phrenic nerve* is entirely void of any myelin sheaths while the axis cylinders are better preserved though also unequal in width and fragmented. The spaces between the axis cylinders are filled with compound granular bodies indicating the acute nature of this process which may have been the immediate cause of death. Figs. 7 and 8, phosphotungstic acid; Fig. 9, Bodian; Figs. 7 and 8 ×300. Fig. 9 ×650.

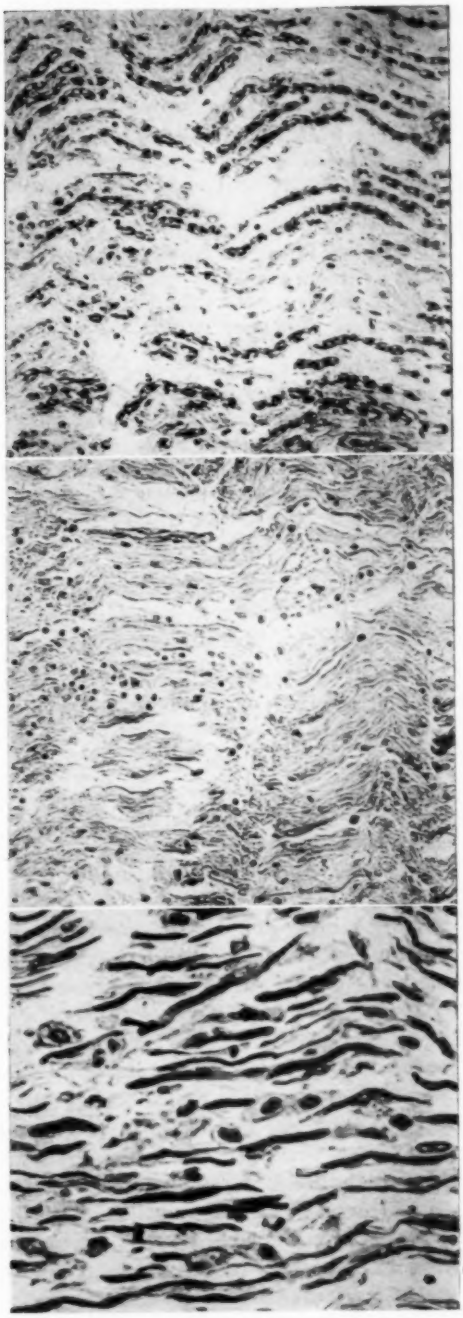

Fig. 7.

Fig. 8.

Fig. 9.

Figs. 7-9.—*(For legends see opposite page.)*

granular layer. In the cortex itself a number of nerve cells were in "chronic disease," others were lost, and in some places the cortical layers were warped but without loss of architecture. The cerebellum was normal. The anterior horns of the spinal cord were diseased in varying degree in different segments. The anterior horn nerve cells were decreased in number, the glia fibers proliferated. In the cervical cord (Fig. 6) a severer degenerative process with cavity formation was present. Hemosiderin was deposited around the blood vessels and a perivascular gliosis had been formed. This process seemed to have been terminated several weeks prior to death and to have been purely degenerative. The posterior roots more than the anterior showed swelling and degeneration of the myelin sheaths, especially in the lumbar cord. The thick fibers appeared more diseased than the thin ones. Schwann's cells were in proliferation but neither glia nor mesodermal tissue had formed a marked scar. The sacral roots of the cauda equina showed the severest changes (Figs. 3 and 4). The majority of their nerve fibers were partially or completely demyelinated, many axis cylinders unraveled, swollen, and fragmented, the Schwann system in marked proliferation. Bundles of very small nerve fibers were numerous but gave no indication as to whether they represented regenerated nerve fibers. The right and left splanchnic nerves showed essentially the same changes though to a lesser degree. The only place where signs of recent, acute disease with the accumulation of numerous compound granular bodies could be demonstrated was in the phrenic nerves. Here, too, inflammatory signs were absent but the blood vessel walls were thickened. The right phrenic nerve (Fig. 7) showed a great number of fairly well-preserved myelinated axis cylinders among others which had lost their myelin. In the left phrenic nerve no myelin was left (Fig. 8) while among its swollen and fragmented axis cylinders an abundance of scavenger cells were visible (Fig. 9). This histologic picture of a peracute disintegration of the respiratory nerve might offer an explanation for the sudden and unexpected death of the child.

The pathological diagnosis was: late stage of peracute polyneuro- and radiculopathy with fresh exacerbation in phrenic nerve and degenerative processes in spinal cord and cortex.

DISCUSSION

The comparable pathologic material of the two cases, namely the sacral roots, is so identical in every detail that it may have easily been from one and the same person: It presents a peracute disintegration of the myelin and axis cylinders of the nerve fibers, without any proliferation of microglial or mesodermal cell elements: compound granular bodies, leucocytic or lymphocytic infiltration; a minor degree of edema and a mild mesodermal scar formation. Its result had been evident to the naked eye in the arachnitic constriction of the cauda equina. In other words, we find the classical picture of a fulminant polyneuropathy such as may be found under manifold conditions of infectious, metabolic, or toxic origin. Nothing can be construed as characteristic of any specific disease or syndrome.

Up to this point the two cases are comparable. This does not mean that they are necessarily different beyond it, but we cannot make any

statement about it since we fail to know the condition of the spinal cord and brain of our surviving patient. No doubt that the encephalopathy, the necrosis in the anterior horns, and the degeneration in the white matter of the spinal cord of the child correspond with the changes described in Landry's ascending paralysis.

It is true that Landry's paralysis has never been a pathologic or clinical disease entity. Pièrre Marie and Tretiakoff have differentiated its two main types, one with preponderant polyneuropathy and radiculopathy, the other with preferential participation of the spinal cord. (Landry's own first patient seems to have had beriberi.) If we are willing to accept this definition, no space is left for another classification of the available material. Absence of infiltration of the meninges and roots in our two cases (so often reported in Landry's form and so rare in the Guillain-Barré syndrome) cannot be recognized as a differential diagnostic characteristic since most of the Landry cases came to necropsy in the first five days of the disease while the scant pathologic specimens of the Guillain-Barré syndrome were gained many weeks after its onset.

Clinically, the two patients appeared very much alike, and the marked changes in the cerebral cortex and the spinal cord of the child came to us as a complete surprise. This raises seriously the question as to whether the individual operated on may not harbor similar asymptomatic alterations in his central nervous system. The absence of clinical signs of involvement of the spinal cord is obviously not sufficient proof against their presence. If this assumption were correct, the last hope of differentiating the groups of Landry and of Guillain-Barré by pathologic anatomic means would have crumbled.

What is, after all, left of the original Guillain-Barré syndrome since Guillain himself has rescinded it so thoroughly and deprived it of all its former characteristics? As far as I can see, there remains only the generally accepted experience that there occur small epidemics of polyneuropathies and radiculopathies with occasional encroachment upon the spinal cord, the brain stem and cortex, possibly of viral etiology, some of which are amazingly benign despite their threatening initial appearance, while others show a high mortality. Why, then, do internists, pediatricians, and neurologists alike still spend so much time in discussing the justification of classifying a patient under the heading of the Guillain-Barré syndrome? Probably there is no other reason than that strange-sounding words, even in our rationalistic time, still cast a magic spell and tend to captivate our phantasy.

Nevertheless, it may be more practical to accept the popular designation and to redefine it than to replace it by six or more long, awkward, and purely descriptive titles. It is to be expected that with our increasing knowledge of the etiological factors more and more disease entities will be dropped from the present group. In the meantime it seems a convenient solution of the dilemma to retain the name Guillain-

Barré syndrome as a general heading, without any attempt at differentiation, for the various forms of polyneuro- and radiculopathy of unknown etiology with or without encroachment upon the central nervous system but with partial block of the spinal fluid as indicated by the albuminocytologic dissociation.

SUMMARY

1. Two representative cases of the Guillain-Barré syndrome are clinically described and their histopathologic findings discussed. One patient was successfully operated upon for adhesive arachnitis and two diseased sacral roots removed for examination. The other patient died unexpectedly in the fourth week of the disease of an acute degeneration of the phrenic nerves.

2. The sacral roots in both cases showed an identical pathologic picture, namely a peracute radiculopathy of almost necrotic nature. The myelin was pulverized and in many instances completely dissolved, the axis cylinders fragmented. No infiltration, no compound granular bodies, and only a scant scar formation from the endoneurium was found. Necropsy in the child revealed, in addition, a polyneuropathy with acute exacerbation in the phrenic nerves, cerebral arachnitis, cortical derangement, necroses in the anterior horns and degeneration in the white matter of the spinal cord, all of which had failed to produce clinical signs.

3. The clinical picture and the pathologic findings did not suggest that either case deserved classification under a special heading.

4. Guillain, Barré, and Strohl had originally believed that patients with a severe but eventually benign polyneuropathy, with preferential involvement of the motor nerves, and albuminocytologic dissociation in the spinal fluid might be united in one group. In 1937, Guillain himself revoked this opinion without reservation.

5. It is suggested we retain, nevertheless, the designation Guillain-Barré syndrome which has become popular as a general heading for the various forms of polyneuropathy and radiculopathy of unknown etiology, with or without encroachment upon the central nervous system and with a partial block as indicated by the albuminocytologic dissociation in the spinal fluid.

REFERENCES

1. Guillain, G., Barré, J. A., and Strohl, A.: Bull. et mém. Soc. méd. d. hôp. de Paris **40**: 1462, 1916.
2. Bradford, J., Bashford, E., and Wilson, J.: Quart. J. Med. **12**: 88, 1918.
3. Casamajor, L.: Arch. Neurol. & Psychiat. **2**: 608, 1919.
4. Taylor, E. W., and McDonald, C. A.: Arch. Neurol. & Psychiat. **27**: 79, 1932.
5. Gillespie, J. B., and Field, E. H.: J. PEDIAT. **14**: 363, 1939.
6. Hyland, H. H., and Russel, W. R.: Brain **53**: 278, 1930.
7. Gaertner, W.: Deutsche Ztschr. f. Nervenh. **123**: 18, 192, 1931.
8. Strauss, I., and Rabiner, A. M.: Arch. Neurol. & Psychiat. **23**: 240, 1930.

8a. Hecht, M. S.: J. PEDIAT. 11: 743, 1937.
8b. Mettel, H. B.: J. Michigan M. Soc. 23: 47, 1924.
9. Guillain, G.: Arch. Neurol. & Psychiat. 36: 975, 1936.
10. De Jong, R. N.: Arch. Neurol. & Psychiat. 44: 1044-1068, 1940.
11. Gilpin, S. F., Moersch, F. P., and Kernohan, J. W.: Arch. Neurol. & Psychiat. 35: 937, 1936.
11*a*. Discussion to this paper.
12. Bassoe, P.: Arch. Path. 26: 289, 1938.
13. Guillain G.: J. belge de neurol. et de psychiat. 38: 322, 1938.
14. Balduzzi, O.: Riv. di pat. nerv. 51: 1, 1938.
15. Roseman, E., and Aring, C. D.: Medicine 20: 463, 1941.

CALCIFICATION OF THE INTERVERTEBRAL DISCS IN CHILDHOOD

H. Stephen Weens, M.D.
Atlanta, Ga.

INTRODUCTION

In recent years the part played by the intervertebral discs in diseases of the spine has received increasing attention. Though excellent studies[1, 2, 3] have contributed a great deal to our knowledge of the anatomy and physiology of the intervertebral cartilages, not all of their pathologic conditions have been completely clarified. The etiology and clinical significance of calcification of the intervertebral discs have thus remained the subject of controversy.

Calve and Galland[4] first observed this process clinically in an adult patient and attributed definite symptoms such as back pain and limitation of motion to this finding. In subsequent case reports a similar opinion was expressed regarding the clinical importance of this observation.[5, 6, 7] Barsony and Koppenstein[8] noted, however, that calcification of the intervertebral discs may also occur in the absence of clinical symptoms. Schmorl,[9] whose fundamental work in this field is generally recognized, considers calcification of the intervertebral discs as an essentially degenerative process of no clinical significance. Most recent reports agree that calcification of the intervertebral discs in adults may occasionally cause vague complaints or may occur in complete absence of clinical symptoms.

The literature reveals that in a small number of instances calcification of the intervertebral discs has been observed in childhood.[10-14] Contrary to observations in adult life it is remarkable that, in all these cases, rather prominent clinical signs and symptoms were noted. The question, therefore, will arise whether calcification of the intervertebral discs in childhood may not be of much more clinical significance than the same process in adult life. Closely linked with this question is the problem as to whether the etiologic factors causing the intervertebral calcification in childhood are not different from those leading to the same phenomenon in later life.

It shall be the purpose of this paper to record the case of a child in whom calcification of a cervical disc was observed in association with rather striking clinical features. An attempt will be made to evaluate the observed findings in comparison with similar cases recorded in the literature and to discuss briefly the etiologic factors which may have

From the Department of Roentgenology Grady Hospital and Emory University School of Medicine.

played a part in this process. It is hoped that this report may stimulate interest in this subject and lead to further observations.

CASE REPORT

D. B., a 5-year-old girl, was admitted to Grady Hospital complaining of marked pain in the back of her head and neck. There had been slight aching of the neck for about two months, but there was no aggravation of these symptoms noted until five days prior to admission when she began to walk with stooped shoulders. Since this time she had developed severe pain in the back of the neck and opposed any effort to move her head. The patient was seen one day before admission in the outpatient department where a tentative diagnosis of myositis was made, and a novocain injection of the neck muscles was done without giving relief.

Fig. 1.—Lateral view of cervical spine (day of hospital admission). Dense calcification in anterior half of intervertebral disc between sixth and seventh cervical vertebrae.

The patient was born as a full-term infant of normal delivery. On several occasions she was admitted to the outpatient department with the diagnosis of tonsillitis, otitis media, and ascariasis. There was no history of trauma and the family history was noncontributory. Eight months before the present admission she had spent ten days in the hospital with follicular tonsillitis.

The temperature on admission was 100° F. and the pulse rate was 120. On physical examination rather conspicuous hyperextension of the neck was noted. Slight passive rotation of the head was possible, but flexion of the head could not be carried out. The patient would

walk with stooped shoulders and marked kyphosis of the dorsal spine. Palpation of the neck was not remarkable except for the presence of a few small lymph nodes. Both eardrums were slightly hyperemic. The heart and lungs did not reveal any remarkable findings and the neurologic examination was entirely negative. Without treatment the temperature returned to normal after two days. After two more days all pain had disappeared and the patient was discharged twelve days after admission free of any symptoms. There was no residual deformity of the spine noted and movement of the head and neck was not restricted.

Laboratory Findings.—A blood count on the day of admission revealed a normal erythrocyte count. The leucocyte count was 8,200 with 1 per cent basophiles, 24 per cent eosinophiles, 33 per cent polymorphonuclear leucocytes, 37 per cent lymphocytes, and 5 per cent monocytes. A second blood count eight days after admission revealed a leucocyte

Fig. 2.—Slight oblique view of cervical spine (day of admission).

count of 11,400 with 1 per cent basophiles, 10 per cent eosinophiles, 59 per cent polymorphonuclear leucocytes, 29 per cent lymphocytes, and 1 per cent monocytes. The urine examination of a voided specimen showed several leucocytes per high power field and was otherwise not remarkable. The Kahn test of the blood serum was negative. A spinal fluid examination one day after admission showed the following values per 100 c.c. of fluid: protein, 17 mg.; sugar, 67 mg.; chlorides, 720 mg. There were no cells noted. The Kahn test and the mastic reaction were negative. The tuberculin test, the trichinella test, and the agglutination series for typhoid fever, typhus fever, and brucellosis were negative. A stool examination revealed no parasites or ova.

Roentgenologic Examination.—Film studies on the day of admission and one day after admission revealed a dense, flocculent, cone-shaped area of calcification, measuring 6 by 5 by 2 mm. in diameter, in the space between the sixth and seventh cervical vertebrae (Figs. 1 and 2). This calcification extended from the anterior portion of the intervertebral disc into its mid-portion. The cervical spine was hyperextended and there was no narrowing of the intervertebral spaces or bone destruction demonstrated. Fluoroscopic examination confirmed the radiographic impression. There was no swelling of the retrotracheal soft tissues seen and the esophagus, on examination with barium meal, did not appear remarkable.

On a chest roentgenogram taken several months prior to admission the calcification was already present and possibly somewhat larger (Fig. 3). A re-examination of the cervical spine twelve days after hospital admission showed that the calcification was considerably decreased in size (Fig. 4). There remained only a small calcium deposit, measuring not more than 1 mm. in diameter, in the region of the anterior portion of the disc. Further roentgenographic studies after four months revealed complete disappearance of the calcification.

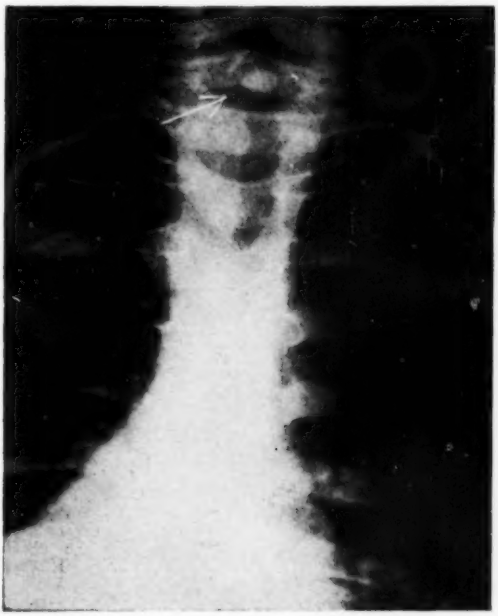

Fig. 3.—Chest film seven months prior to hospital admission showing calcification in region of intervertebral disc between sixth and seventh cervical vertebrae.

COMMENT

A 5-year-old child developed a sudden episode of severe pain in the back of the neck, associated with hyperextension of the cervical spine, kyphosis of the dorsal spine, and marked limitation of motion of the

head and neck. The acute episode was preceded by slight aching in the back of the neck of two months' duration. The previous history revealed frequent attacks of tonsillitis, otitis media, and ascariasis.

Slight fever and leucocytosis with eosinophilia were noted. The eosinophilia could hardly be evaluated in view of the history of ascariasis. There were no other significant laboratory findings observed and the neurologic examination was entirely negative.

The x-ray examination revealed a dense calcification involving the nucleus pulposus and anterior portion of the annulus fibrosus of the sixth cervical disc. This calcification had been present for at least seven months as demonstrated on a previous chest roentgenogram.

Fig. 4.—Lateral view of cervical spine (twelve days after admission). Marked decrease in size of calcification.

Without treatment complete recovery followed within twelve days. X-ray examination after this interval revealed very striking decrease in the size of the calcification which remained as a minute deposit in the region of the annulus fibrosus. The adjacent vertebrae did not show significant pathologic changes. A re-examination after four months showed complete disappearance of the calcification.

It is highly suggestive that the rapid change in the size of the calcification and the rather pronounced clinical symptoms are the manifestations of a common pathologic process involving the sixth cervical disc.

In the following are five cases which are abstracted from the literature available to us:

I. *Case Report of Baron*[10].—A 12-year-old boy whose past history was not remarkable took sick with influenza-like symptoms. The patient developed fever up to 101.3° F. and complained about backache. On the tenth day of the disease this pain became very severe and was associated with marked kyphosis. During the next days the fever went down and the pain disappeared. Four weeks after onset of symptoms the patient had completely recovered without residual spinal deformity. The physical examination was entirely negative except for a slight tenderness on pressure over the lower dorsal and upper lumbar vertebrae. The Mantoux test and the Wassermann reaction were negative. The sedimentation rate was 32 mm. per hour. A blood count showed a leucocyte count of 12,000 with a relative lymphocytosis. The first x-ray examination, eighteen days after onset of symptoms, revealed a rather large and dense calcification in the center of the disc between the twelfth dorsal and first lumbar vertebrae, and a smaller calcification in the midportion of the disc between the first and second lumbar vertebrae. A second x-ray examination after four months showed that the calcification of the discs was possibly slightly larger. Another re-examination after one year revealed that the calcium deposits had disappeared.

II. *Case Report of Kohlmann*[11].—A 12-year-old boy complained suddenly about backache after calisthenics. There was slight tenderness over the spinous processes of the upper dorsal spine. Since the pain did not disappear with bed rest an x-ray examination of the dorsal spine was done after several days. The examination revealed a dense calcification in the center of the disc between the fourth and fifth dorsal vertebrae. After two months a very marked decrease in the size of the calcification was noted. The back pain disappeared after several weeks. There were no laboratory findings included in this brief case report.

III. *Case Report of Lyon*[12].—An 8-year-old boy complained suddenly about pain in his neck and inability to move his head, which he kept inclined toward his right side. The patient had high fever of two days' duration during which time he kept his right arm quiet in order to avoid pain in his neck. The past history of the patient revealed an episode of "grippe" and otitis media two years prior to the present disease. Four days after onset of symptoms he was able to move his arm again and after twelve days there was apparently complete clinical recovery. The first x-ray examination, three weeks after onset of symptoms, showed a dense bean-sized area of calcification in the region of the nucleus pulposus between the sixth and seventh cervical vertebrae. After five months definite diminution of the size of the calcification was noted and after another three months the calcification had disappeared.

IV. *Case Report of von Held.*[13]—A 10-year-old child who had been in good health became ill with a cold and fever. After one week the child developed pain in the left shoulder, neck, and head accompanied by marked limitation of motion. The neurologic examination was entirely negative. On physical examination the tonsils were found to be somewhat reddened and covered with exudate. The neck appeared stiff and hyperextended and the head was kept inclined to the left side.

The x-ray examination (after about two weeks) revealed rather dense calcium deposits in the intervertebral discs between the second and

third, third and fourth, and the fifth and sixth cervical vertebrae. After conservative treatment the complaints of the patient disappeared within two months. A roentgenologic examination after two and one-half months disclosed a nearly complete disappearance of the calcification.

There were no laboratory studies included in this case report.

V. *Case Report of Keyzer.*[14]—A 2½-year-old boy who had been in good health took suddenly sick with severe pain in the neck and head and high fever. There was marked stiffness of the neck which slowly subsided during the hospital stay of several weeks. The physical examination was essentially negative and there were no clinical findings of meningitis.

The laboratory studies revealed a leucocyte count of 14,000 with an essentially normal differential count. The intracutaneous tuberculin test and an agglutination series for typhoid fever were negative. A blood culture taken during the febrile course disclosed hemolytic streptococci. After a febrile course of five weeks complete recovery took place. The patient was treated with a plaster-of-Paris jacket.

The first roentgenologic examination about one month after onset of symptoms revealed calcification in the anterior halves of the discs between the second and third, third and fourth, and the fourth and fifth cervical vertebrae. These vertebrae did not show evidence of destruction or periosteal reaction. Subsequent roentgenologic studies after an interval of several months did not show significant changes.

SUMMARY OF CLINICAL FINDINGS

These six cases are characterized by a number of interesting clinical symptoms and signs. In all patients an episode of pain in the back or neck was encountered which corresponded topographically to the segment of the spine showing the intervertebral calcification. These painful episodes would last from two weeks to several weeks and were associated with the development of a rather marked deformity of the spine. Limitation of the motion of the neck and head was noted in the cases in which calcification of the cervical discs was observed. The spinal deformity was a transient process and a return to normal condition was recorded in all cases in a relatively short time. In four of the six cases the painful course of the disease was accompanied by mild or high fever which lasted from a few days to five weeks. The author's patient had slight fever of two days' duration while being observed in the hospital. In none of the patients was a positive tuberculin reaction recorded. A negative agglutination series for typhoid fever was recorded in two cases. In Keyzer's[14] patient a blood culture revealed the presence of hemolytic streptococci. The blood count was reported in four cases and disclosed the presence of leucocytosis. In the author's case eosinophilia was noted but this finding can hardly be evaluated in view of the history of ascariasis. The sedimentation rate was found to be elevated in two of the patients.

COMMENT

Calcareous deposits may be found in various portions of the intervertebral discs and vary considerably in their clinical importance with

their location. It is beyond the scope of this paper to give a detailed anatomic description of the intervertebral discs, but for better understanding of the pathologic processes it shall be briefly stated that the discs consist of three integral parts: The nucleus pulposus, annulus fibrosus and cartilage plates. The nucleus pulposus is a gelatinous structure which contains a network of fibers and remnants of the notochord. It occupies an eccentric position in the middle of the disc, being localized more anteriorly in the cervical and lumbar spine and more posteriorly in the dorsal spine. The nucleus pulposus is enclosed from above and below by the cartilage plates which border the adjacent vertebral bodies. The annulus fibrosus surrounds the nucleus pulposus like a capsule. It is differentiated from the nucleus pulposus by its more abundant and much coarser fibers. The annulus fibrosus apparently provides strength and shape to the nucleus pulposus which, on account of its resiliency, has a shock-absorbing function.

Calcareous deposits in the annulus fibrosus are rather frequently encountered according to the studies of Schmorl[9] and Ratheke.[15] These calcium deposits are usually localized in the peripheral layers of the annulus fibrosus and are, as a rule, so small that they are not demonstrated on roentgenological examination during life. They are frequently found in patients with spondylosis deformans. Larger, rather heavy calcium deposits are, according to Schmorl, localized in the nucleus pulposus and it is this type of calcification which has been usually reported in the literature under the heading of intervertebral calcification and which shall be the subject of our discussion. In the cases we have summarized and in our case the rather heavy calcification involved the nucleus pulposus. However, as Barsony and Koppenstein[8] pointed out, this nuclear calcification may extend into the region of the annulus fibrosus as it was noted in our patient.

As stated in our introduction calcification of the intervertebral discs is occasionally encountered in routine examinations of adult patients who are entirely free of clinical symptoms. Schmorl[9] and Ratheke,[15] on the basis of post-mortem studies, demonstrated that calcification of the nucleus pulposus was not infrequently observed with increasing age. They claimed that such a finding was not the result of a process which had given rise to symptoms during life.

The five summarized cases and the case which we have described differ in certain aspects from the observations of Schmorl and Ratheke. Whereas four of these six cases showed calcification of the nucleus pulposus of the cervical discs, involvement of the cervical spine was not encountered by these authors. Furthermore, in Schmorl's and Ratheke's series calcification of the nucleus pulposus was not found in young individuals.

Though the number of the cases in which calcification of the nucleus pulposus was demonstrated in childhood is small, we believe that in view of the rather striking clinical features the significance of this finding cannot be lightly dismissed. Whereas calcification of the nucleus

pulposus seems to be of minor clinical importance in adult life, it may be of definite clinical significance in childhood. This difference may offer an explanation if we consider the etiology of the calcification of the intervertebral discs.

Schmorl,[9] on the basis of extensive pathologic studies, claimed that calcification of the nucleus pulposus is a degenerative process. The question arises, however, as to what could cause these degenerative changes. Calcification, as the result of the physiologic and pathologic aging of the intervertebral discs, could hardly be expected to occur in childhood; however, this mechanism may very well operate in adult life and may be an important factor in the development of intervertebral calcification in older age groups. Trauma was of doubtful significance in one of the summarized cases. It could be postulated that the calcification may be due to some type of general metabolic disorder or vascular disease. The fact, that only one or a small number of discs were affected in the cases which we have described, seems to disprove such a conception. Calcification as the result of an aseptic necrosis, comparable to similar processes in bones, is, however, a definite possibility.

Baron[10] expressed the opinion that calcification may be the result of a metastatic infectious process involving the discs. This viewpoint was supported by Lyon[12] and von Held.[13] In favor of this theory is the observation that in those cases, in which calcification of the nucleus pulposus was seen in childhood, signs of infection such as fever, leucocytosis, pain, and increased sedimentation rate were noted. Boehmig[16] has demonstrated that the disc in childhood is supplied by a regular number of blood vessels which penetrate into the cartilage plates. These vessels undergo a slow process of degeneration, beginning rather early in life and terminating in the third decade. He called attention to the fact that the discs in a young individual are thus connected with the general circulation and are open to invasion by any disease which may be propagated by the blood stream. In this connection it appears remarkable that in five of the six cases observed in childhood a considerable decrease in the size of the calcification or complete disappearance of the calcareous deposits was noted. In Baron's patient almost complete disappearance of the calcification was seen within one year. Lyon[12] reported resolution of the deposits in eight months. Kohlmann's[11] and von Held's[13] patients showed considerable reduction in the size of the calcification within two months. In our case a striking diminution was observed in two weeks and complete absorption after four months. Such rapid change in the calcification indicates a rather active metabolism as provided by the ample blood supply of the juvenile disc. Contrary to this phenomenon, calcification of the intervertebral discs in adults is a stationary process and changes in the calcification are only rarely observed.

The question may arise as to how rapid such calcification of the nucleus pulposus may develop. This question is difficult to answer inas-

much as none of the patients had a roentgenological examination at the very onset of the symptoms. In our case it was demonstrated that the calcification already existed at a time when the patient was apparently symptomless. Baron[10] and Barsony and Koppenstein[8] suggested that such a process may be quiescent for a considerable length of time. They drew attention to the fact that a similar phenomenon may be observed in calcification of bursae. Carnett[17] has clearly demonstrated that a calcified bursa may remain symptomless for a long period of time until the onset of an acute episode of pain. His observations likewise show that calcium deposits in this condition may rapidly disappear after such an acute attack. Analogous to this process it seems possible that calcification of an intervertebral disc is a sign of a slowly progressing degenerative process. At any time an intercurrent process, such as infection or trauma may cause a disturbance of the local tissue metabolism of the disc resulting in relatively rapid changes of the calcium deposits and production of symptoms which eventually lead to clinical discovery of this phenomenon.

SUMMARY AND CONCLUSIONS

Calcification of the intervertebral discs involving the nucleus pulposus is described in six cases occurring in childhood. Five of these cases were recorded in the literature and one patient was observed by us. All cases were characterized by an acute episode of pain in the region of the involved segment of the spine, limitation of motion, and spinal deformity.

In the absence of pathologic studies it is not possible to arrive at definite conclusions as to the etiology of this phenomenon in childhood. However, signs and symptoms of infection were noted in most of the cases and suggest that an inflammatory process was associated with the calcification. The fact that the intervertebral discs in childhood possess a blood supply may be important in this connection. The intervertebral discs are thus open to any disease carried by the blood stream. An aseptic necrotic process as a possible cause of the calcification is mentioned.

The number of observed cases is too small to form definite impressions. The observed cases suggest, however, that there exist certain differences between calcification of the intervertebral discs in childhood and in adult life.

1. Involvement of the cervical spine was noted in four of six cases occurring in childhood. Calcification of the nucleus pulposus in adult life is localized predominantly in the dorsal spine and lumbar spine.

2. Rapid change in the size of the calcification or complete absorption was noted in five of the six described cases. Calcification of the nucleus pulposus in adult life is, as a rule, a stationary process.

3. Rather striking clinical symptoms were encountered in the cases described in childhood. Calcification of the nucleus pulposus in adult life is probably of little clinical significance.

In all cases complete recovery was noted.

The recognition of this syndrome appears important in view of the differential diagnosis of meningitis, myositis, and diseases involving the vertebrae or spinal cord.

REFERENCES

1. Beadle, O. A.: Medical Research Council Special Report Series No. 161, London, 1931.
2. Schmorl, G., and Junghanns, H.: Die gesunde und kranke Wirbelsaeule im Roentgenbilde, Leipzig, 1932, Georg Thieme.
3. Keyes, D. C., and Compere, E. L.: J. Bone & Joint Surg. **14**: 897, 1932.
4. Calve, J., and Galland, M.: J. de radiol. et d'electrol. **6**: 21, 1922.
5. Lyon, E.: Fortschr. a. d. Geb. d. Röntgenstrahlen **39**: 76, 1929.
6. Horenstein, V.: Fortschr. a. d. Geb. d. Röntgenstrahlen **35**: 713, 1927.
7. Rietema, L. P., and Keijser, S.: Acta radiol. **9**: 606, 1928.
8. Barsony, T., and Koppenstein, E.: Fortschr. a. d. Geb. d. Röntgenstrahlen **41**: 211, 1930.
9. Schmorl, G.: Fortschr. a. d. Geb. d. Röntgenstrahlen **40**: 18, 1929.
10. Baron, A.: Jahrb. f. Kinderh. **104**: 357, 1924.
11. Kohlmann, G.: Verhandl. d. deutsch. Röntgen-Gesellsch. **23**: 48, 1931.
12. Lyon, E.: Ztschr. f. Kinderh. **53**: 570, 1932.
13. Von Held, H. J.: Deutsche Ztschr. f. Chir. **242**: 675, 1934.
14. Keyzer, J. L.: Maandschr. v. kindergeneesk. **8**: 467, 1939.
15. Rathcke, L.: Fortschr. a. d. Geb. d. Röntgenstrahlen **46**: 66, 1932.
16. Boehmig, R.: Arch. f. klin. Chir. **158**: 374, 1930.
17. Carnett, J. B.: Surg., Gynec. and Obst. **41**: 404, 1925.

POSTWAR DEVELOPMENTS IN CHILD HEALTH STUDY IN GREAT BRITAIN

ALAN MONCREIFF,* M.D., F.R.C.P.
LONDON, ENGLAND

THE past twenty-five years in Britain have seen the curious paradox of a steady improvement in the health of almost all children combined with a growing dissatisfaction with the medical services available for the care of children. This period has been one of great expansion in the child welfare services for the care of the young infant, and much original work has appeared from individual pediatricians on subjects of importance in the study of diseases of children. Yet these two streams of the medical care of the young have been flowing apart. On the one hand, the medical officers in the child welfare and school medical services have received little training in pediatrics, and the hospital pediatrician was either not interested or not allowed to be interested in the care of the child in health.

Behind all this lay the fact that pediatrics had little or no academic recognition. The subject received only scant attention in either the curriculum or the final examination of medical students, yet often a third or more of a general medical practitioner's work dealt with sick children. It has been estimated that for every £100 ($400) allotted each year in grants to the provincial universities of England and Wales, only 5½ pence (about 10 cents) was spent on the special teaching of child health.

Recent developments indicate that this unsatisfactory state of affairs is coming to an end. The new departments of child health in the University of Durham and Liverpool, the promised development of an Institute of Child Health in London, together with the steady growth of existing departments in Edinburgh and Glasgow, all show that there is a new awakening of interest in the care of the child.

Historically, the work in Glasgow and in Birmingham may be mentioned first. In the former, a Chair in Medical Paediatrics was founded in 1924, a special lectureship having existed since 1919, but although the staff includes four lecturers and three assistants in addition to the professor, there is no direct cooperation between the University Department of Paediatrics and the Local Authority (that is, the local government) as regards child welfare work or the school medical service. Yet most valuable work has been achieved in Glasgow, most notably the research on rickets, carried out by the first holder of the university chair and his colleagues.

*Physician to Out-Patients at the Hospital for Sick Children, Great Ormond Street.

In Birmingham, a chair and a department of pediatrics grew out of suggestions put forward in a memorandum dated 1925 but cooperation with the authorities for the preventive work among children has not been achieved. Here again important contributions to the study of disease in children have been carried out, especially in the nature of anemia in early life. In addition, at the Children's Hospital in Birmingham, a building, especially designed for the care of infants, fully furnished, with all the most recent equipment, has been opened since the war began and affords a most promising center for the investigation of such important problems as infantile diarrhea.

In Edinburgh the history of recent developments dates from 1931 when a university chair in "Child Life and Health" was endowed and a department slowly developed which now is staffed by a part-time professor with a lecturer and three assistants and the staff of the Royal Edinburgh Hospital for Sick Children as university teachers. A particular feature of the Edinburgh Department has been close association with the Maternity Hospital for a study of the newborn infant, for the neonatal mortality (deaths in the first month of life) has not shown the improvement achieved at other age periods of childhood and still remains far above that obtaining in other cities and other countries. From the first in Edinburgh, the City Corporation has offered facilities for the training of medical students and the senior Medical Officer for Child Welfare is associate-physician to the Maternity Hospital and takes part in the routine work and teaching at the Infant Clinic there.

Those responsible for more recent developments have profited by these experiences in England and Scotland. In 1942 the Nuffield Provincial Hospitals Trust made a substantial grant to the University of Durham for a Department of Child Health. This has now been opened in the University Medical School, King's College, Newcastle-upon-Tyne, with clinical departments in the Royal Victoria Infirmary and the Babies' Hospital. New building is impossible during the war and at present the department centers round the Children's Clinic in the grounds of the Royal Victoria Infirmary. The clinic comprises the outpatient clinic, special clinics, a child welfare center, research laboratory, and department library.

In addition to the professor, the medical staff normally will consist of two assistants and two resident medical officers, full-time, with two assistant physicians, part-time. Close relationship with local authorities is achieved in several ways. The Professor of Child Health is a member of the Maternity and Child Welfare Committee of the Newcastle Health Committee, and the chief Child Welfare Medical Officer of Newcastle is a member of the staff of the Babies' Hospital. Students obtain experience of child welfare clinics both in the department of child health and in the city.

The latest academic development in the field now being described, is the establishment of a Department of Child Health in the University

of Liverpool. Here there has been a happy collaboration between the University, the City Corporation, and a voluntary hospital, the Royal Liverpool Children's Hospital. A professor of child health has been appointed to a part-time chair and he will be director of the department with headquarters at Alder Hey Hospital, a large municipal hospital for children. This will afford not only important clinical, research, and teaching facilities to supplement those available at the voluntary children's hospital but will also give access to certain prophylactic clinics such as infant welfare, tuberculosis, child guidance, and rheumatism clinics. Furthermore, the neonatal work of the Liverpool Maternity Hospital will continue to be available for teaching and research purposes. In addition to the director, the medical staff will consist of the present three university lecturers in clinical pediatrics, two assistants, three registrars, and several senior residents. Salaries have been met by joint arrangements between the University, the City Corporation and the voluntary hospitals concerned.

It is likely that other universities in Britain will shortly announce developments on similar lines. In Manchester it is proposed to form a center for child health and pediatrics with a chair and close association with all child health services in the city.

It is in London, however, that the greatest interest is centered in possible developments. It may seem strange that there has been hitherto no academic recognition of the subject in the metropolis and little or no cooperation of the children's hospitals and departments in the teaching hospitals with the preventive services of the various municipal and local authorities.

It has just been announced, however, that the trustees of the Nuffield Foundation have allocated £100,000 ($400,000) for a chair of child health in the University of London and that it is proposed to create a postgraduate Institute of Child Health. This will be associated with the Hospital for Sick Children, Great Ormond Street, and the Obstetric Department of the British Postgraduate Medical School at the Hammersmith Hospital of the London County Council.

Full details of the proposed institute are not available but it has been stated that it will rank as a central teaching establishment of the University with a building adjoining the existing hospital buildings at Great Ormond Street, already largely reconstructed on modern lines. The chairman of the hospital has indicated the contemplated scope of the new Institute by naming the figure of £250,000 ($1,000,000) as the sum necessary for a suitable site and building. Here it should be possible to train workers in the field of child health and by close association between the institute and the hospital, ensure a better cooperation between the medical and nursing personnel concerned in child care, both in health and disease, than has been achieved hitherto.

Among the special problems likely to be studied at such an institute may be included the following: (a) Management of the premature

baby. The death rate in the first month of life has not been reduced by anything like the same degree as the death rate in the first year. It has been estimated that about half the deaths in the first month are associated with premature birth and it is felt that a co-ordinated study could introduce means to save far more of these babies than at present. (b) Nutrition. Wartime necessity has greatly increased the available knowledge on nutrition and such knowledge must be applied in detail to the needs of children. (c) Physiotherapy. Rehabilitation in childhood is at the beginning of a new and intensely interesting phase. Correct posture must be more carefully studied and remedial exercises given a better scientific background.

All these problems concern those working among healthy children just as much as those working in hospitals and thus the two diverging streams of curative and preventive pediatries are being brought together again under the aegis of academic recognition of the supreme importance of the subject of child health for the future welfare of the community.

American Academy of Pediatrics

Proceedings

THIRTEENTH ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

St. Louis, Mo., Nov. 9-11, 1944

Symposium on Parenteral Therapy

PARENTERAL ADMINISTRATION OF AMINO ACIDS*

Alexis F. Hartmann, M.D.
St. Louis, Mo.

THE *theoretical* basis for the parenteral administration of amino acids rests upon the following considerations:

1. Protein molecules in living tissues are constantly being broken down and rebuilt by synthesis from amino acids.

2. Amino acids enter also into the formation of important nitrogenous substances, such as hormones, vitamins, enzymes, and other physiologically active compounds.

3. Only about one-half of the twenty-three known amino acids can be synthesized in normal metabolism.

4. Normal health and body function are certainly incompatible with gross and prolonged amino acid depletion.

5. Less severe and even transient deficiencies are probably also deleterious and should be prevented whenever possible. In fact we believe that the parenteral administration of "amigen" is indicated in any condition in which it is difficult or impossible to provide full nutritional requirements in the natural way.

6. "Amigen" contains all the essential amino acids necessary both for positive nitrogen balance and growth when administered orally or parenterally.

In the *practical* administration parenterally of "amigen," the following points may be mentioned:

1. Properly prepared material may safely be injected intravenously, subcutaneously, and intraperitoneally.

2. Too rapid intravenous administration first produces a facial flush and a sensation of warmth, then a spreading flush over the body with

Part of the symposium presented before the annual meeting of the American Academy of Pediatrics, St. Louis, Mo., Nov. 9-11, 1944.

*In this discussion, it should be borne in mind that our remarks refer to but one preparation of amino acids—the enzymatic (pancreatic) digest of casein prepared under the direction of Dr. Warren M. Cox by Mead Johnson and Company, and furnished under the trade name of "Amigen" (accepted by the Council of Pharmacy and Chemistry of the American Medical Association). Almost all of our clinical experience has been with this preparation, and a review of the literature indicates that this preparation was also used in most of the experimental and clinical studies made elsewhere.

nausea, vomiting, and sometimes fever. To avoid such reactions a slow intravenous drip is recommended; when the patient's face begins to flush then drip should be slowed. A rate below .01 Gm. per kilogram per minute is probably best.

3. Absorption from the peritoneal cavity is so rapid that symptoms characteristic of too rapid intravenous administration may result.

4. In infants the subcutaneous route is very much to be preferred, because it is technically much easier and the rate of absorption is always slow enough to avoid the reactions described and approximates absorption from the intestine after feeding. When given by this route, material adjusted to pH 6.5 should be used.

5. "Amigen" may be combined with glucose solutions, Ringer's solution, and lactate-Ringer's solutions for subcutaneous administration. The mixture used most extensively has been that comprising equal parts of 10 per cent "amigen," 10 per cent glucose and lactate-Ringer's solution.

6. With poor peripheral circulation as in severe dehydration or the presence of very low plasma protein, the subcutaneous administration of any hypertonic solution differing much from the electrolyte composition of normal body fluids is contraindicated. Such solutions tend to remain where injected and withdraw water and electrolytes from the blood and intercellular fluid. Frequently an initial intravenous injection overcomes such difficulties.

7. From the quantitative point of view, the following is an example: Suppose a young infant weighing 5 kg., whose water needs are not abnormal, needs parenteral feeding. His requirements may be summarized as follows:

Caloric requirement	= 100-120 Cal. per kilogram body weight
Protein requirement	= 3-4 Gm. per kilogram body weight
Carbohydrate	= 3-15 Gm. per kilogram body weight
Water	= 150-300 c.c. per kilogram body weight

In attempt to meet such requirements, it should not be difficult to give every 8 hours, or three times in 24 hours, 250 c.c. subcutaneously of a mixture of equal parts of 10% "amigen," 10% dextrose, and lactate-Ringer's solution, followed each time by 100 c.c. (20 c.c. per kilogram) of 10% dextrose intravenously.

Total intake could then be summarized as follows:

Protein	= 25 Gm. = 5 Gm. per kilogram body weight (adequate)
Carbohydrate	= 55 Gm. = 11 Gm. per kilogram body weight (adequate)
Water	= 1050 c.c. = 210 c.c. per kilogram body weight (adequate and not excessive)
Calories	= 320 = 65 per kilogram body weight (approximately ½ of total requirements)

Minerals will be balanced from the acid-base point of view and adequate

It would be easy by subcutaneous, intramuscular, or intravenous injection to supply vitamins C and A and the B complex group. To provide "essential" fatty acids and as yet unknown factors in small but probably sufficient amounts, "enriched" plasma may occasionally be given intravenously in the customary dosage of approximately 20 c.c. per kilogram body weight.

If a condition of excessive water loss prevailed because of vomiting, diarrhea, or fistula, larger quantities of fluid and, therefore, food could easily be administered, and total caloric requirements could possibly be met.

PARENTERAL REPAIR OF DEHYDRATION

S. Z. Levine, M.D.
New York, N. Y.

DR. BUTLER and Dr. Hartmann have reviewed the maintenance requirements of infants and children and their coverage by parenteral therapy when oral intake is impracticable. They outlined the routes of administration, the manner and rate of injections, and the types and amounts of fluid commonly used.

The parenteral repair of body dehydration poses a different problem. By definition, dehydration signifies a reduction in total volume, often with alterations in chemical composition, of body fluids. The two chief aims of parenteral therapy are therefore replenishment of depleted reserves by the provision of fluid over and above maintenance needs and correction of electrolyte and colloid distortions, when present. The magnitude of the negative water balance determines the amounts of fluid needed in treatment; the concurrent loss of solutes, both qualitative and quantitative, the types of solutions.

Common conditions leading to dehydration in infants and children include: total starvation or inadequate fluid intake; gastric vomiting, diarrhea, hemorrhage, excessive sweating, high fever, extensive burns, and polyuria.

Whether the negative water balance results from insufficient intake or excessive outgo via urine, stools, skin and lungs, or vomitus, the usual train of events in body dehydration takes the following course. Water and electrolytes (Na^+, Cl^- and HCO^-_3) are withdrawn from the distensible interstitial fluid compartment into the blood plasma to maintain its volume and electrolyte pattern. This transfer depletes the extracellular fluid reserves and explains the early clinical signs of dehydration—loss of skin turgor, dryness of the skin and mucous membranes and depression of the anterior fontanel. Urinary output is diminished with selective sparing of electrolytes, if necessary, by the concentrating ability of the kidneys without, however, retention of nitrogenous and inorganic waste products. Water is concurrently withdrawn from the cells (with some nitrogen and potassium) to sustain uniform osmotic pressure of the body fluids. Insensible perspiration in this early stage is not reduced because the skin and lungs have a prior claim on available water for vaporization. This obligatory loss of extrarenal water without electrolytes often leads to hypertonicity of the body fluids and probably accounts, in part at least, for the cellular withdrawal of water.

From the New York Hospital and the Department of Pediatrics, Cornell University Medical College.

Part of the symposium presented before the annual meeting of the American Academy of Pediatrics, St. Louis, Mo., Nov. 9-11, 1944.

With further depletion of the extracellular fluid reserves, the water content of the blood plasma falls, resulting in a drop in blood pressure, blood volume and blood flow and a concomitant rise in plasma proteins and colloid osmotic pressure. This sluggish circulation is evident clinically by feeble, rapid heart action, cold, clammy extremities, and oliguria or even anuria. The latter in turn leads to impairment of renal function with retention of the end products of metabolism. Blood studies at this stage often show elevations of nonprotein nitrogen, serum proteins and perhaps chlorides, a lowering of the plasma carbon dioxide content and a high hematocrit and hemoglobin. Water continues to be withdrawn from the intracellular compartment to the extent that it eventually comprises approximately 50 per cent of the total water loss. The solutes, K^+, Mg^{++}, $PO_4^=$, $SO_4^=$ and N, accompany in varying amounts this withdrawal of cellular water and claim water for their excretion in the urine. Coincidentally or subsequently, water is no longer available in sufficient quantities for vaporization from the skin and lungs and the syndrome of dehydration fever develops. The final stage, if the dehydration remains untreated, is exhaustion of the interstitial fluid reserves, profound reduction of plasma volume, extensive depletion of intracellular fluid and protoplasmic death.

Just as the magnitude of the negative water balance determines the extent of body dehydration, so are the qualitative alterations in chemical composition of the body fluids determined by the accompanying loss of electrolytes, protein or both. The latter losses, both qualitative and quantitative, vary with the pathogenesis of the dehydration and the routes of elimination.

For example, more Cl^- than Na^+ is lost in gastric vomiting. If the vomiting is marked or of long duration, the loss of Cl^- may be of such magnitude that selective renal tubular reabsorption cannot prevent hypochloremia; the Na^+ which is released combines with HCO_3^- to raise the bicarbonate content of blood plasma and a metabolic alkalosis results. Its recognition, clinically, is facilitated by the presence of shallow, irregular respirations, muscular hypertonicity, exaggerated tendon reflexes, and the characteristic signs of tetany. Blood studies, if performed, will show an elevation of plasma bicarbonate and a reduction of plasma chlorides.

Conversely, proportionately more fixed base (cations) than acid (anions) is usually lost in the stools in infantile diarrhea. Superposed on this alimentary loss of base is the frequent accompaniment of oliguria with retention of acid waste products. Blood analysis in the first instance may show a reduction of both plasma bicarbonate and chloride; if the second mechanism predominates, the fall in plasma bicarbonate is associated with a rise in chloride. In general, both of these mechanisms contribute in varying degree to the metabolic acidosis so commonly observed in the dehydration of infantile diarrhea. In

the absence of blood measurements, acidosis should be suspected clinically if the respirations are deep and exaggerated and no basis for respiratory alkalosis is present.

Similarly, loss of blood in hemorrhage often culminates in hypoproteinemia, and starvation per se superposes ketosis on body dehydration. If ketosis is marked, it may simulate metabolic acidosis clinically but an acetone odor may be detected in the breath and ketone bodies appear in the urine.

Finally, it is theoretically possible, although infrequently seen in practice, for a pure state of simple contraction of body fluid volume without structural change to occur as a sequel to negative balances of water and solutes in proportions qualitatively similar to those normally existing in the body fluids. Blood measurements would reveal merely a reduction in total blood volume with no distortions of colloid or electrolyte patterns.

Parenteral repair requires the provision of fluids in amounts sufficient to restore the total volume of body fluids to normal levels and the use of solutions of appropriate composition to correct any of the above chemical derangements, if coexistent.

Clinical signs of dehydration in infants become manifest when fluid depletion approximates from 8 to 12 per cent of the body weight (80 to 120 c.c. per kilogram). More extreme states result in greater losses (200 c.c. per kilogram or more daily in severe diarrhea). In general, 200 to 250 c.c. of total fluids per kilogram of body weight, rarely more, by the parenteral route will suffice during the initial one or two days of starvation; 140 to 150 c.c. per kilogram per day, thereafter. Hypodermoclyses and intravenous infusions are preferred over the intraperitoneal route; treatments may be intermittent at four- to six-hour intervals or by continuous intravenous drip. The intermittent method is ordinarily used at the New York Hospital and the daily routine during the period of starvation consists of one to two clyses, each of 40 to 50 c.c. per kilogram; two to three intravenous infusions, each of 30 c.c. per kilogram, and one transfusion of whole blood or plasma of 20 c.c. per kilogram. This routine is subject to revision under special circumstances, but with the employment of appropriate solutions, the recommended amounts are usually adequate for restoration of depleted body fluid volume.

The types of fluids selected for treatment depend on the causation of the dehydration with especial reference to the relative magnitude of losses of water and solutes, and the condition of the patient. This information is readily obtainable from a careful history, physical examination and serial blood analyses for the constituents previously enumerated.

The following solutions have proved effective for restoration of body fluid and electrolyte volume: isotonic saline (0.85 per cent); Ringer's (potassium, calcium and magnesium in addition to sodium chloride in

the proportions normally contained in blood plasma); Locke's and Tyrode's (Ringer's solution plus sodium bicarbonate in different quantities). These fluids may be used interchangeably; isotonic saline possessing the advantages of simplicity of preparation and proved effectiveness, especially in acute dehydration.

Correction of electrolyte distortion leading to a metabolic acidosis may be achieved directly or indirectly. The direct approach entails the initial use of a bicarbonate ($NaHCO_3$) or lactate ($CH_3CHOHCOONa$) solution (one-sixth molar) as a partial or total replacement for isotonic saline. This procedure is especially indicated in the forms of metabolic acidosis due primarily to loss or fixed base (low plasma bicarbonate and low chloride). The advantages of M/6 sodium lactate over bicarbonate are simplicity of preparation, stability and less potential hazard of inducing alkalosis; however, in circulatory failure, liver damage and extreme anoxia, the lactate may be oxidized exceedingly slowly if at all and bicarbonate is preferred in these conditions.

The indirect approach for combating metabolic acidosis calls for the re-establishment of copious urinary flow and the promotion of selective renal excretion of acid waste products (Cl^- and other anions). This purpose is readily served by the intravenous infusion of a hypertonic dextrose solution (10 per cent) in distilled water or isotonic saline, administered rapidly, and preceded by a clysis of isotonic saline alone or a mixture of dextrose (2.5 per cent) in saline. The form of metabolic acidosis especially amenable to this therapy is associated with a lowered plasma bicarbonate content and an elevated chloride (respiratory alkalosis which gives a similar distortion of the electrolyte pattern of plasma may be ruled out from the history and examination and, if necessary, by determination of blood pH).

In severe acidotic states, and particularly if blood measurements are unobtainable, the combined approach is perhaps optimal. In such cases, the initial one or two treatments consist of subcutaneous injections of isotonic saline and M/6 sodium lactate (or sodium bicarbonate) solutions in proportions of 2:1 or 1:1, followed by intravenous infusions of hypertonic dextrose solution. Calculation of the bicarbonate (or lactate) requirement from the level of the plasma carbon dioxide content gives variable results and is usually unnecessary.

Following initial correction of the acidosis, body dehydration per se is treated by subsequent clyses and infusions of isotonic dextrose (5.5 per cent) and saline (or Ringer's) solutions, given separately or together in the indicated amounts. The former solution serves the purposes of avoiding excess administration of sodium chloride of correcting the ketosis of starvation and of reducing the metabolism of body protein and the consequent output of nitrogenous end products and extra water claiming excretion in the urine. The latter solutions, if excess is avoided, help to maintain the isotonicity and electrolyte pattern of the body fluids in the presence of normal renal function.

Saline and dextrose solutions are similarly effective for combating the metabolic alkalosis of gastric vomiting and the concurrent ketosis of starvation.

Correction of a complicating anemia or hypoproteinemia requires transfusions of whole blood or plasma, respectively.

The routine, as outlined, is usually adequate for the repair of the effects of acute dehydration. Persistence of this state beyond several days demands parenteral supplementation with vitamins, particularly thiamine (10 mg.) and ascorbic acid (100 mg.), and amino acids (Amigen) in the form of a buffered enzymatic casein hydrolysate, especially if blood plasma is not available. It is important to stress that oral feedings should be reinstituted as early as feasible.

DISCUSSION

DR. ALLAN M. BUTLER, Boston, Mass.—Dr. Levine mentioned the administration of volumes of saline. They are entirely different from the volumes of saline I mentioned. I was talking about maintenance therapy and not repair. Dr. Levine was talking about repair. Repair requires large amounts of saline, maintenance but little.

DR. JEROME L. KOHN, New York, N. Y.—When you start feeding these children, how soon do you start, do you feed frequently, do you give oral feedings and how much, and if so, how soon do you begin?

DR. BUTLER.—I am sure 100 people would answer that question in fifty different ways. The way we answer it in our clinic is to say, start your oral feedings when you are still giving parenteral fluids. In the meantime you do not have to think about giving adequate fluids and having adequate calories orally. You can then start with very small amounts. The frequency is decided by the manner in which the patient takes them. If you say, we are through with parenteral feedings and we will start oral feedings, you will frequently find that you will give more orally than the patient can handle which may again start up the diarrhea and vomiting. I cannot be too emphatic about beginning the oral feedings while you are still giving the parenteral fluids.

DR. ALEXIS F. HARTMANN, St. Louis, Mo.—I would like to answer this question this way. If this were an extremely sick child, very toxic, vomiting a lot, then I believe that complete withholding of anything by mouth is indicated, but we are rapidly turning from that point of view as far as oral medication is concerned, except as Dr. Butler said. What we have been using routinely for the last three or four years has been an isotonic mixture of 10 per cent amigen, 10 per cent dextrose, and substituting for lactate Ringer's solution, sodium lactate one-half per cent. We find this sort of food seems to be absorbed quickly.

DR. JEROME L. KOHN.—Is it possible to give too much fluid?

DR. BUTLER.—I think it is very possible, because if such babies are given fluids too rapidly, particularly by the intravenous route, they are prone to have pulmonary edema. A number of autopsies have shown fluid in the pleural cavity in very large amounts.

DR. FEDERICO SANTOS GÓMEZ, Mexico City.—I would like to know, when you start feeding the child do you start with carbohydrate or protein?

DR. BUTLER.—That is a question which would be answered in various ways by various people. I do not believe there is any one answer. Ordinarily when you start feeding, you have two objectives, one which I am sure is in the mind of Dr. Alexis Hartmann, first, of bringing the pH low enough to bring the body in normal environment, and second, you give by mouth what you cannot give parenterally. I see little use of giving salt and glucose in your oral feedings. Those you can give very satisfactorily parenterally. Give in your oral feedings in small quantities the substances which make for tissue repair in the body.

DR. SAMUEL Z. LEVINE, New York, N. Y. (closing).—I have not much to add except to emphasize one point with respect to the two questions that were asked. Obviously the answer depends upon the cause of the dehydration. If as Dr. Hartmann mentioned, vomiting is the cause or diarrhea is the cause, and those are the two most common causes, one must be particularly careful not to upset the intestinal tract by giving food. I know by unfortunate experience in treating organic paralysis in the newborn, particularly in the premature group, that if you institute early oral feedings too rapidly you will produce recurrence of the diarrhea sufficiently severe to cause death. If, on the other hand, you withhold food orally until the infants have not had stools for from twelve to twenty-four hours, your results will be definitely better.

The Pediatrician and the War

Dr. Geoffrey W. Esty of Warfield, N. J., has been promoted to the rank of Major in the Army.

Eighteen of the members admitted to the Academy at the November meeting are serving with the Armed Forces. They are as follows:

Army

Captain Hugh A. Carithers, Jacksonville, Fla.
Captain Charles W. Cory, Saginaw, Mich.
Major George D. Doroshow, Los Angeles, Calif.
Major Frederick H. Fehlmann, San Diego, Calif.
Major Leo Grossman, Bronx, N. Y.
Captain Salmon R. Halpern, Dallas, Texas.
Captain Edward Adams Hardy, Pelham, N. Y.
Major Martin J. Harris, Louisville, Ky.
Captain Paul Herzog, Kenosha, Wis.
Captain Ng William Hing, Puerto Rico.
Major Robert Marvel Keagy, Altoona, Pa.
Captain Charles E. Muhleman, La Porte, Ind.
Captain Harry Strongin, Brooklyn, N. Y.
Captain Arnold Widerman, Philadelphia, Pa.

Navy

Lieutenant Commander Leonard B. Outlar, Wharton, Texas.
Lieutenant Harold Arthur Rosenberg, Jackson Heights, N. Y.
Lieutenant (jg) Edward V. Turner, Wilmington, N. C.
Lieutenant Alvin B. Williams, San Jose, Calif.

Dr. James W. Britton of Anniston, Ala., has been retired from active military duty because of physical disability.

News and Notes

Meeting of the Children's Bureau Advisory Committee on Maternal and Child Health

At the meeting held in Washington Dec. 7, 8, and 9, 1944, a number of recommendations made by the various subcommittees were adopted. Some of these are of considerable interest to the pediatricians.

The *Subcommittee on Maternity Care* urged the delivery of all women in good hospitals, although they recognize that there are serious pediatric problems to be considered in caring for infants in congregate nurseries and called attention to the fact that there has been an increase in hospital deliveries from 37 per cent in 1935 to 68 per cent in 1942.

They urged the building and development of maternity units as part of general hospitals and that a well-equipped nursery, including a nursery for premature infants, is indispensable as part of the maternity unit.

The subcommittee urged the re-establishment of the educational activities of the Children's Bureau providing postgraduate and medical courses in obstetrics.

The *Subcommittee on Child Health* recommended the adoption of the recent report which was presented at the American Academy of Pediatrics meeting in November. As this has been printed in detail in the JOURNAL (**25**: 625, 1944) it will not be reprinted in this report.

They added, however, two additional recommendations to the report which are as follows:

1. An educational program is needed to teach the public to utilize child health activities.

2. The Children's Bureau should develop a unit on school health which in cooperation with the office of education would carry out the recommendations in this report relating to the school health program.

In addition, the subcommittee made two other recommendations which are as follows (Recommendations III and IV):

RECOMMENDATION III

> The Committee recommends that in the interest of harmonious and effective execution of various programs within the several States, serious consideration be given by the Children's Bureau to the importance of establishing a sound basis of understanding with the medical and allied professions since these are the groups which must play a major role in the carrying out of such programs.

RECOMMENDATION IV

> The Committee approves the general principle that scales of remuneration be based entirely on professional preparation and merit without discrimination on other grounds.

The *Subcommittee on Services for Crippled Children* recommended as follows in regard to services for children with rheumatic fever:

1. Services to children with rheumatic fever or heart disease under the State crippled children's programs should be expanded and that, to this end, additional appropriation of Federal funds A and B under title V, part 2, of the Social Security Act should be sought by the Children's Bureau. Additional State appropriations are also needed.
2. Before a rheumatic fever program is inaugurated or expanded in a State, qualified medical, medical-social, and public-health nursing services should be available.
3. The qualification standards previously recommended for professional personnel who provide services in State rheumatic fever programs should be maintained in expansion of the programs.
4. The Children's Bureau should approve State rheumatic fever programs only if they provide a range of services including case finding, diagnostic services, and medical, medical-social, and nursing supervision in clinics, suitable institutions, foster homes, and children's own homes, and only if provision is made for continuity of care, including adequate follow-up services.
5. The Children's Bureau should explore methods for securing from the States information that can be used in evaluating the results of these programs. It is suggested that the Council on Rheumatic Fever be requested to assist in the evaluation of these programs.
6. Steps should be taken to insure the training of professional —medical, medical-social, and nursing—personnel in the field of rheumatic fever in children.

The E. Mead Johnson Awards

In 1938 an offer by Mead Johnson and Company to establish the "E. Mead Johnson Award" for a term of ten years was accepted by the Academy. The conditions and terms of the award which were published in the January, 1939, number of the JOURNAL (**14**: 135, 1939) are as follows:

1. Two awards, one of $500 and one of $300, will be given annually at the annual meeting of the Academy of Pediatrics.

2. The awards will be made for research work published during the previous calendar year.

3. There is no limitation as to the type or scope of the research except that it be in the field of pediatrics.

4. The award is limited to workers in the United States and Canada.

5. The award shall be limited to investigators who have been graduated not more than 15 years previous to the publication of the research.

6 There is no restriction as to the journal of publication of the research.

The Committee interprets 2 and 5 as follows:

The award in 1939 will be given for research published during the period Jan. 1, 1938, through Dec. 31, 1938, by a graduate of 1923 or later. The award in 1940 will

be given for research published Jan. 1, 1939, through Dec. 31, 1939, by a graduate of 1924 or later, and so on for subsequent years.

Heads of departments and hospital services are requested to call attention to investigations meeting the requirements of the award and *in particular to research work in the field of pediatrics published in other than pediatric journals.* At present communications should be addressed to the chairman.

The awards have been as follows:

1939	First	Dr. Franklin H. Gibbs of Boston for his studies in electroencephalography.
	Second	Dr. Dorothy Andersen of New York for her studies on cystic fibrosis of the pancreas.
1940	First	Dr. Robert E. Gross of Boston for his work in the surgical treatment of ductus arteriosus.
	Second	Dr. Lee E. Farr of Wilmington, Del., for his studies of protein metabolism in the nephrotic child.
1941	First	Dr. R. J. Du Bos of New York in recognition of his studies on microbial antagonisms.
	Second	Dr. Albert B. Sabin of Cincinnati in recognition of studies on viruses.
1942	First	Drs. David Bodian and Howard Howe of Baltimore for their joint studies on poliomyelitis.
	Second	Drs. Harold E. and Helen Harrison of Chicago for their joint studies on the pathogenesis of rickets.
1943	First	Dr. Hattie E. Alexander of New York in recognition of her contribution to the treatment of *Hemophilus pertussis* infections.
	Second	Dr. Philip Levine of Newark, N. J., for his studies on the Rh factor.
1944	First	Dr. Fuller Allbright of Boston in recognition of his studies on the skeletal and metabolic disturbances in hyperparathyroidism, hypoparathyroidism, rickets, and other diseases affecting bone formation and the processes of calcification.
	Second	Dr. Josef Warkany of Cincinnati for his studies on the development of malformations.

The authorities of the State of New York have accepted the filing of the certificate of incorporation of a new national child care organization which under the title, ***Foundation for Child Care and Nervous Child Help, Inc.,*** will start its activity with the beginning of 1945.

Among the plans the new foundation intends to pursue is a school for several hundred mentally subnormal children in New York City, a national institution for prepsychiotic and predelinquent children, a school for social workers and nurses for mentally subnormal children,

regular courses and forums for instruction of parents and teachers, and finally two serial publications: one devoted to the problems of care of mentally abnormal children and the other to adult educational readers on similar subjects.

Among the Foundation's Directors are: Dr. Harry Bakwin, New York University Medical College; Dr. Violet De Laszlo of New York City; Dr. J. Louise Despert, Cornell Medical College; Dr. George Henry, Cornell Medical College; Dr. Ernest Harms, Editor of the Journal, *The Nervous Child;* Dr. Leo Kanner, Johns Hopkins University, Medical School, and Justice Jacob Panken of New York City. Dr. Leo Kanner will serve as president and Dr. Harms as executive director for the first period; Helen L. Buttenwieser is the counselor for the Foundation.

Montevideo, Nov. 10, 1944.

Dr. Borden S. Veeder,
Editor, The Journal of Pediatrics,
St. Louis.
Dear Sir:

In March, 1945, forty years will have passed since the founding of "Archivos Latino-Americanos de Pediatría," a pediatric journal founded in 1905 by Luis Morquio, Gregorio Aráoz Alfaro, Fernandes Figueira, and Olinto de Oliveira and published in Buenos Aires from 1905 to 1929.

As the appearance of this periodical, the first international one on pediatrics in Latin America, marks an epoch, since from that time the problem of the child has taken shape in these countries, a group of Uruguayan doctors, representing the institutions of pediatrics and child care, has organized an executive committee in order to commemorate this fortunate happening.

Two of the illustrious founders have died, the eminent professors Morquio and Fernandes Figueira, but happily Aráoz Alfaro in Buenos Aires and Olinto de Oliveira in Rio de Janeiro are functioning at the height of their intellectual activities; therefore this committee believes homage ought to be paid by the pediatricians of America to these four illustrious colleagues.

With this object we ask your adherence and ask that you publish this note. We take advantage of the opportunity to greet you with the highest esteem.

Yours very truly,
ROBERTO BERRO
President

VÍCTOR ESCARDÓ Y ANAYA
Secretary

The following were certified by the *American Board of Pediatrics* at the examination held by the board in New York City on Dec. 17, 1944:

Captain Fred Harold Allen, Station Hospital, Bradley Field, Conn. (formerly Holyoke, Mass.)
Dr. Erna Goettsch Anderson, 266 Beacon St., Boston, Mass.
Dr. Alta Ashley, 4 Abbott Road, Wellesley Hills, Mass.
Dr. Samuel Righter Berenberg, 411 E. 69th St., New York, N. Y.
Dr. Ubaldo L. Bizzarri, 1100 Park Ave., New York, N. Y.
Dr. James T. Cameron, 1400 Hancock, St., Quincy, Mass.
Dr. David Jerome Cohen, 3 Colony St., Meriden, Conn.
Dr. Edward Michael DiTolla, 445 West 23rd St., New York, N. Y.
Dr. Hania Wislicka Ehlers, 1014 St. Paul St., Baltimore, Md.
Dr. Helene Eliasberg, 420 West End Ave., New York 24, N. Y.
Lieutenant Marcus E. Farrell, U. S. Naval Training Station, Epidemiological Unit No. 12, Sampson, N. Y. (formerly Clarksburg, W. Va.)
Dr. William H. Fost, 107 Franklin St., Belleville, N. J.
Dr. Paul Freud, 106-15 Queens Blvd., Forest Hills, N. Y.
Dr. Benjamin Goldsmith, 42-06 159th St., Flushing, N. Y.
Dr. Jacob Greenblatt, 67 Forest St., Stamford, Conn.
Dr. John Robert Heafey, 84 West Ave., South Norwalk, Conn.
Lieutenant Bernard John Houston, Port Dispensary, Brooklyn Army Base Terminal, 58th St. and 1st Ave., Brooklyn, N. Y. (formerly Philadelphia, Pa.)
Dr. Leo Jenkins, 4501 Skillman Ave., Sunnyside, L. I., N. Y.
Lieutenant Chris Peter Katsampes (Navy) Potomac Annex, Bn M & S., 23rd and E. St., N. W., Washington, D. C. (formerly Rochester, N. Y.)
Captain Michael C. Kemelhor, 1258th S.C.S.U., Halloran General Hospital, Staten Island, N. Y. (formerly Brooklyn, N. Y.)
Dr. Althea D. Kessler, McClatchy Building, 69th and Market St., Upper Darby, Pa.
Dr. Jules I. Klein, 816 Monongahela Building, Morgantown, W. Va.
Dr. Max Landsberger, 2181 Seneca St., Buffalo, N. Y.
Dr. Lucille Liberles, 1739 Eutaw Place, Baltimore, Md.
Captain Bernard B. Lilien, Maxwell Field Station Hospital, Montgomery, Ala. (formerly Irvington, N. J.)
Dr. J. Philip Lombard, 402 Ocean Ave., Brooklyn, N. Y.
Dr. Anthony J. Maffia, 212 E. 61st St., New York, N. Y.
Captain William M. McFadden, Port Surgeon, Baltimore Cargo Port of Embarkation, Paca-Pratt Building, Baltimore, Md. (formerly Germantown, Pa.)
Dr. Mark Mohr, 8621 21st Ave., Brooklyn, N. Y.
Captain James P. Morrill, Kelly Field Station Hospital, San Antonio, Texas (formerly Paterson, N. J.)
Dr. Gertrud Clara Reyersbach, Massachusetts General Hospital, Boston, Mass.
Dr. Robert A. Schless, 16th and Walnut St., Philadelphia, Pa.
Dr. Bernard A. Schmierer, 1328 49th St., Brooklyn, N. Y.

Dr. Austin Howard Schoen, 8223 Bay Parkway, Brooklyn, N. Y.
Dr. Lawrence M. Shapiro, 1 West 74th St., New York 23, N. Y.
Dr. Dorothy Louise Shindel, Philadelphia Hospital for Contagious Diseases, Philadelphia, Pa.
Dr. Gertrude Slater, 67 Forest Ave., Stamford, Conn.
Dr. Margaret H. D. Smith, Sydenham Hospital, Harford Road and Herring Run, Baltimore 12, Md.
Dr. Anthony Gerard Stigliano, 514 Bainbridge St., Brooklyn, N. Y.
Lieutenant Caleb O. Terrell, Jr., U. S. Naval Net Fuel Depot, Newport (Melville), R. I. (formerly Fort Worth, Texas)
Dr. Jean Wells, 1018 Farmington Ave., West Hartford, Conn.
Dr. Eleonore C. Zaudy, 45 Orchard Street, Boston-Jamaica Plain, Mass.

At this examination sixty-four applicants were examined; forty-two passed and were certified; twenty failed and two were conditioned in one subject.

Erratum

The name of Dr. Jacques M. Smith was omitted from the December issue of the JOURNAL OF PEDIATRICS in the list of candidates who were elected to active membership in the Annual Pediatric Society at the annual meeting at Atlantic City in September, 1944.